THE American Journal OF Gastroenterology

VOL. 21, NO 3 MARCH, 1954

Nineteenth Annual Convention
Washington, D. C.
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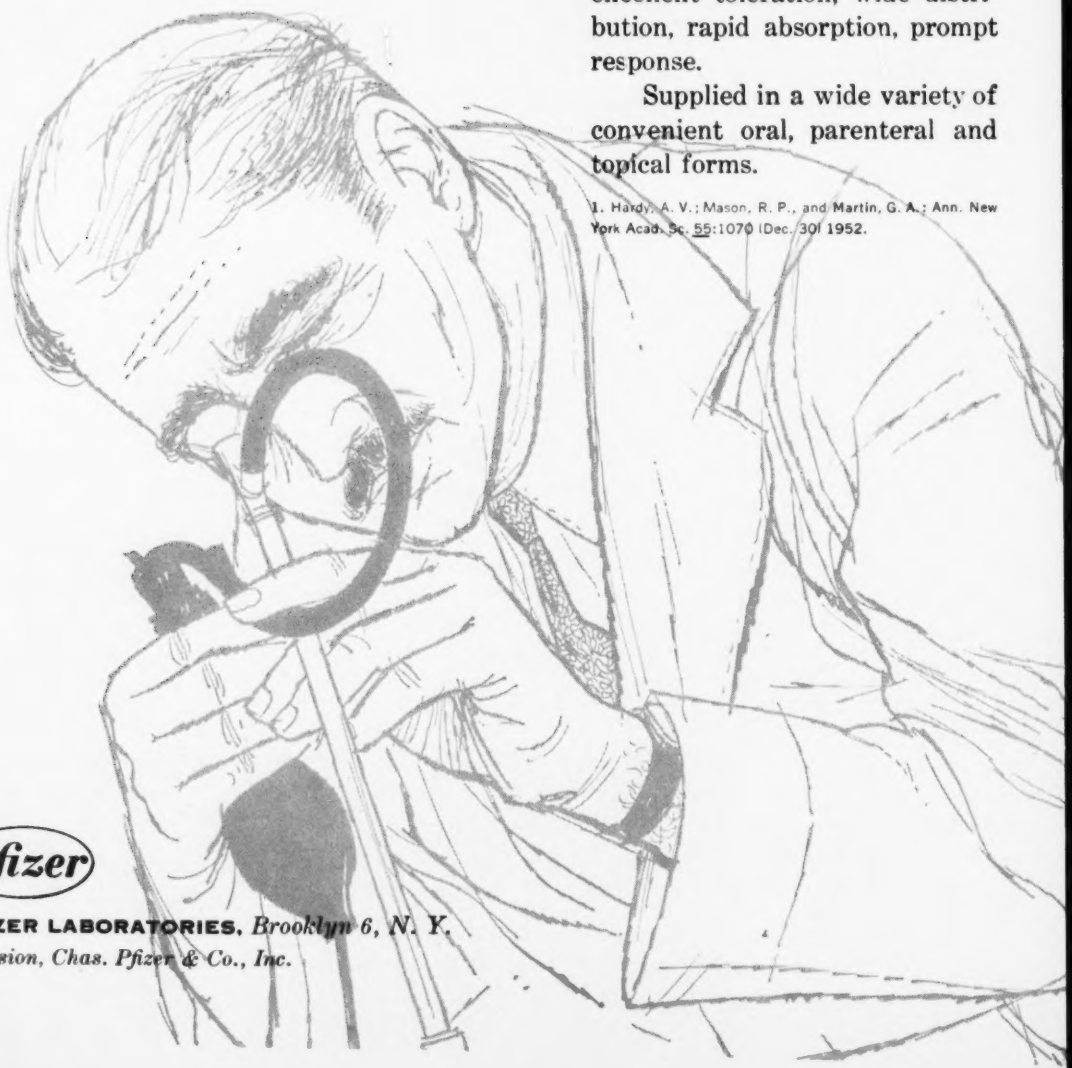

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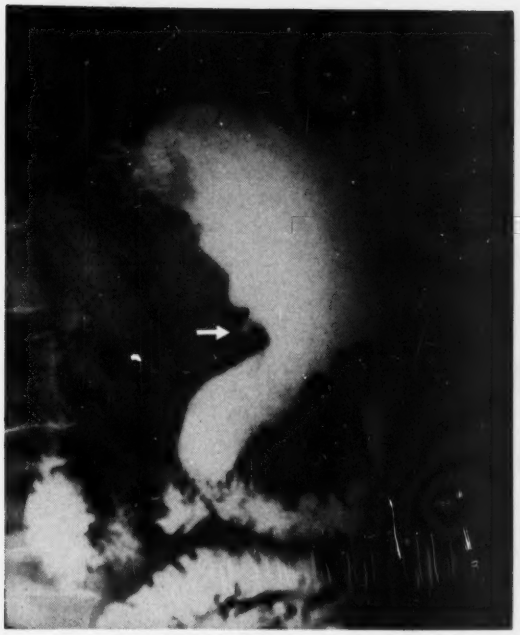

Fig. 1 "Roentgen examination . . . revealed the ulcer to be very much in evidence."

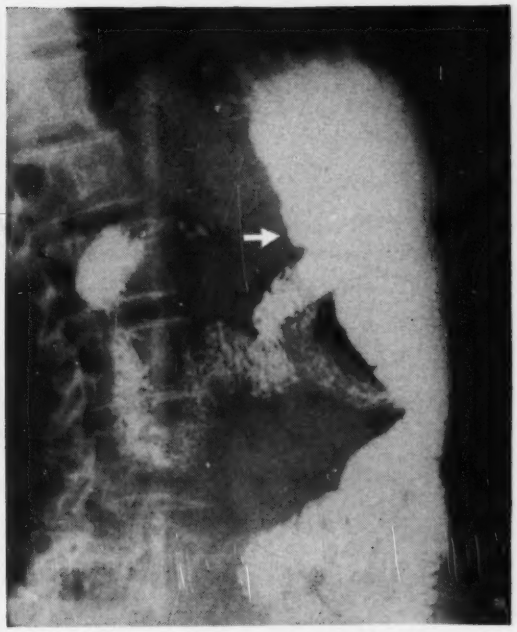

Fig. 2 In ten weeks "the ulcer niche was no longer in evidence roentgenologically or gastroscopically."

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"Ten weeks of controlled regulation was necessary before we were satisfied that the ulcer niche was no longer in evidence roentgenologically or gastroscopically (*Fig. 2*).

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1. Schwartz, I. R.: Personal communication, Feb. 9, 1953.

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THE American Journal OF Gastroenterology

(FORMERLY THE REVIEW OF GASTROENTEROLOGY)

The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

contents:

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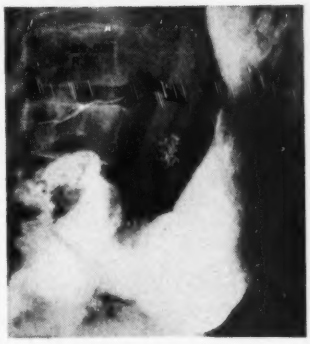

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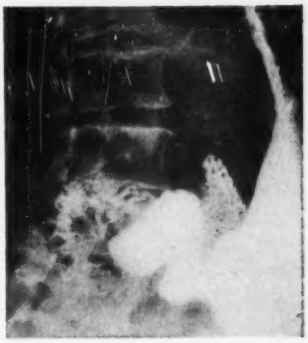

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2. Rogers, M.P., and Gray, C.L.: Am. J. Digest. Dis. 19:180, 1952.

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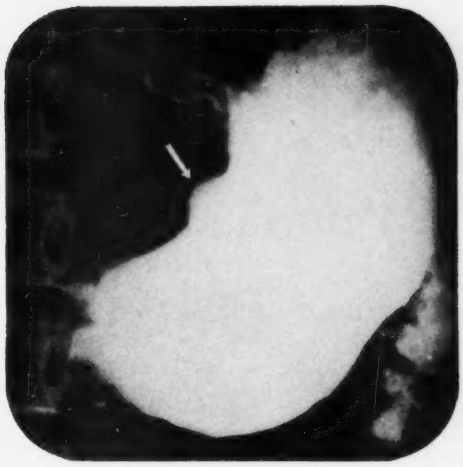

Fig. 3, Case 103 before therapy.

healed with

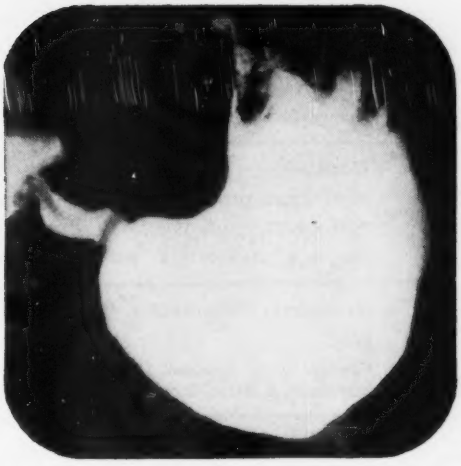

Fig. 6, Case 103 after 4 months PRANTAL therapy.
* Heineken, T. S.: Rev. Gastroenterol. **20**:829, 1953.

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Hunter, C.: Canad. M. A. J. *30*:41 (Jan.) 1934.

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Best, R. R.; Hicken, N. F., and Finlayson, A. I.: Ann. Surg. *110*:67, 1939.

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In chronic cholecystitis, "the bile acid of choice is dehydrocholic acid...."

Cheney, G., in Reimann, H. A.: Treatment in General Medicine, ed. 2, Philadelphia, F. A. Davis Company, 1941, vol. 1, p. 851.

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Sanders, R. L.: Am. J. Surg. *72*:811, 1946.

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Cranshaw, J. F.: Am. J. Digest. Dis. *17*:387, 1950.

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Beckman, H.: Pharmacology in Clinical Practice, Philadelphia, W. B. Saunders Company, 1952, p. 361.

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O'Brien, G. F., and Schweitzer, I. L.: M. Clin. North America *37*:155 (Jan.) 1953.

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VOLUME 21 MARCH, 1954 NUMBER 3

CLINICAL X-RAY STAFF CONFERENCES ON THE COLON*

I. DIFFICULTIES OF RECOGNIZING CARCINOMA IN THE PRESENCE OF DIVERTICULITIS DEFORMITIES

LYNN A. FERGUSON, M.D.
JAMES A. FERGUSON, M.D.
BENJAMIN R. VAN ZWALENBURG, M.D.
and
EDWARD F. DUCEY, M.D.
Grand Rapids, Mich.

INTRODUCTION

The cases presented in the Clinical X-ray Staff Conferences at Los Angeles will be published as a series of short conferences. They will correlate clinical, radiological, surgical, and pathological information just like the weekly X-ray Staff Conference held in many hospitals, but are distilled from the cases seen in our hospital during the past three years. They are for the most part cases which presented particular difficulty of diagnosis or management.

We have been impressed with the occasional difficulty presented by patients who have diverticulitis, both in differentiation between diverticulitis and malignancy and in the diagnosis of small malignant tumors present in an area already deformed by diverticulitis. Our experience indicates that there is in this field a small group of patients with whom extreme care must be taken to avoid important errors of diagnosis. This first section will illustrate problems in this type of case.

Case 1:—A 61 year old man was first seen in August, 1949 with the chief complaint of fresh red bleeding from the rectum occurring with bowel movements during the previous several months. Hemorrhoidectomy had been done elsewhere

*Presented before the Eighteenth Annual Convention of the National Gastroenterological Association, Los Angeles, Calif., 12, 13, 14 October 1953.
From the Ferguson-Droste-Ferguson Hospital, Grand Rapids, Mich.

eight months previously. There was no history of abdominal cramping, weight loss, tarry stools or change of bowel habit.

Abdominal examination was negative and proctosigmoidoscopy showed a normal mucosa and lumen to 22 cm. There was, however, some blood admixed with stool suggesting the presence of an intrinsic abnormality beyond the limit of the 25 cm. instrument. Further studies were recommended.

Obviously, the major effort of the radiologist in this case must be to locate the suspected neoplasm of the colon. Fluoroscopy showed marked deformity of a large area of the mid-sigmoid, characteristic of deformity due to fibrosis

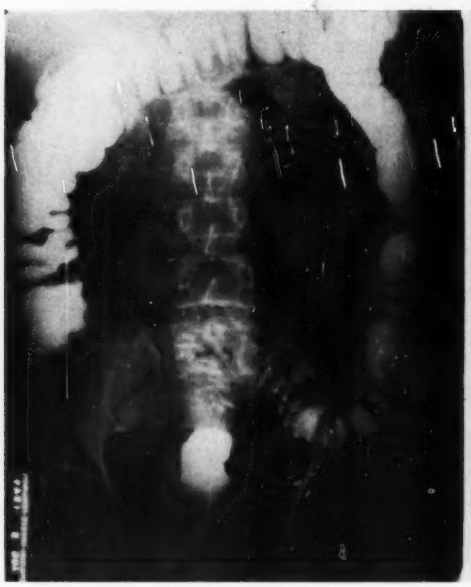


Fig. 1

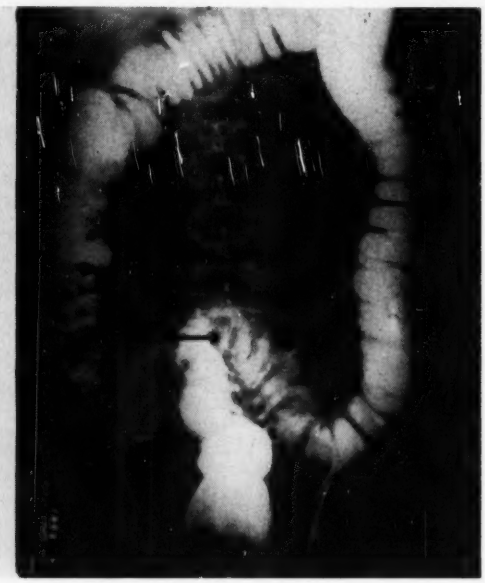


Fig. 2

Fig. 1—Case 1. Barium filling film, representative of the initial examination, demonstrating an evenly distributed diverticulitis deformity of the sigmoid colon.

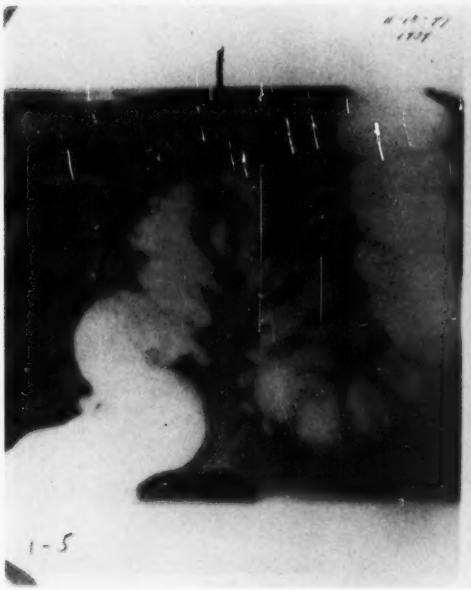
Fig. 2—Case 1. Barium filling film at time of recheck, showing a local variation in the pattern of diverticulitis deformity.

from diverticulitis. There was no tenderness to indicate activity of the process at the time of examination. The barium filling film (Fig. 1) showed a marked irregularity of a long area of the sigmoid together with the presence of a number of diverticula presenting the typical appearance of deformity due to diverticulitis. There was no evidence here of any portion of the deformed area which differed from the other portions in appearance. Air injection films presented evidence only of deformity due to diverticulitis.

Although the patient was otherwise asymptomatic the relatively small amount of rectal bleeding and the finding of blood mixed with stool during sigmoidoscopy could not safely be attributed to the diverticula. We know that diverticula do

bleed but we also know that malignancy is a far more likely and vastly more important source of bleeding. Final diagnosis should therefore be deferred in this situation. A recheck barium enema at three months was recommended as the next step toward final diagnosis. This deliberate deferment of final diagnosis is a most important point in management of this type of case.

The recheck examination three months later (Fig. 2) presented a similar appearance in the barium injection film but the pattern was slightly different at the inferior margin of the topmost loop of the sigmoid. Postevacuation film and air films did not provide additional help. Fluoroscopy, however, had revealed a slight delay in passage of barium past the area in question and a spot film (Fig.



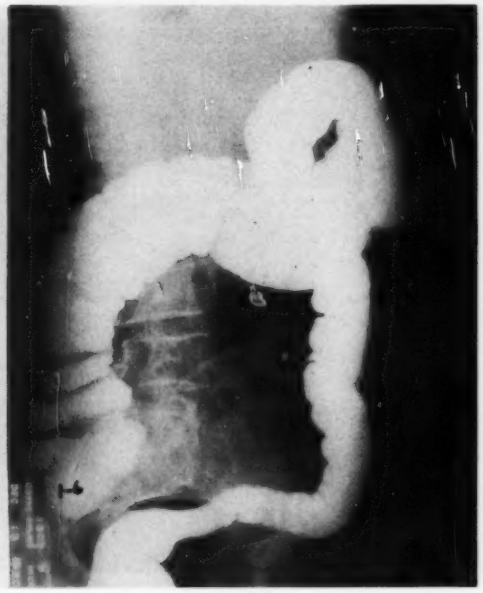


Fig. 3 Fig. 4

Fig. 3—Case 1. Spot film revealing small filling defect at the site of slight delay in initial passage of the barium.

Fig. 4—Case 1. Postoperative film, demonstrating smoothly patent anastomosis with no evidence of recurrence.

3) showed a definite suggestion of a small intraluminal filling defect. Diverticulitis may produce very bizarre types of defects but here was an indication that something in the nature of a small neoplasm must be considered. At this second examination the x-ray evidence suggested a definite possibility of carcinoma.

Final diagnosis still had not been reached but the x-ray findings, previously negative for neoplasm had now altered and suggested a possibility of neoplasm. Resection was therefore done. At operation a small localized mass was found in the sigmoid with some difficulty due to the presence of multiple diverticula and pericolic inflammatory change. A segmental resection of the sigmoid colon with primary anastomosis was performed uneventfully.

The segment of colon removed was 16 cm. long. There was evidence of previous inflammation of several diverticula which were scattered throughout the length of the specimen; no active inflammation of any of these sacs, however, was present at this time. Near the distal end of the specimen a friable, hemorrhagic polyp 18 mm. long was attached to the mucosa by a delicate pedicle; this polyp showed obvious evidence of recent bleeding, and appeared grossly benign. Microscopic examination, however, showed atypical gland formation with sufficient variation in the appearance of individual cells to warrant classification as grade 1 adenocarcinoma; there was early epithelial invasion of the submucous layer. A coronal section through a representative diverticulum showed very little active inflammation but a moderate degree of old fibrosis

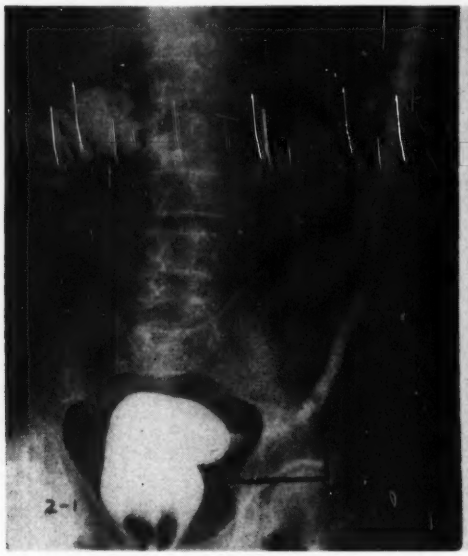


Fig. 5

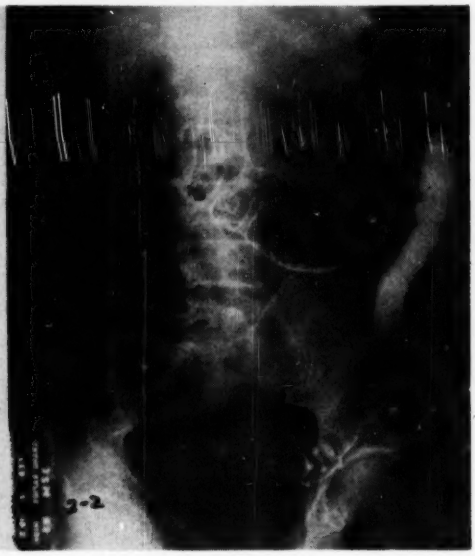


Fig. 6

Fig. 5—Case 2. Barium filling film showing a long area of irregular constriction of the sigmoid colon due to diverticulitis.

Fig. 6—Case 2. Double contrast film demonstrates a short marked constriction within the larger area of diverticulitis. This suggests a small neoplasm.

was present in the pericolic fat. The pathologic diagnosis was "malignant polyp, apparently localized", and "diverticulitis, old".

A single postoperative film (Fig. 4) is presented to demonstrate the very satisfactory appearance of the colon following sigmoid resection. A few very small diverticula are present in the distal descending colon, but the entire area of deformity has been excised and there is no evidence of recurrent neoplasm. The most recent x-ray study was 3½ years following surgery and the satisfactory appearance continues unchanged.

Here then is a situation in which an entirely satisfactory initial x-ray examination presented only evidence of deformity due to diverticulitis. The malignant

polyp would have escaped diagnosis if a recheck had not been made within a reasonable time. The successful management of this case depended on a high index of suspicion on the part of the clinician and on his realization that the radiologist is more apt to miss early carcinoma when diverticulitis is present than in the normal colon.

Case 2:—A 48 year old man was seen in February 1951. He did not have any subjective complaints at that time but had had a bowel obstruction two months previously. Ileostomy had been done and subsequently closed. The patient was then referred to us for review of the situation. Definite diagnosis

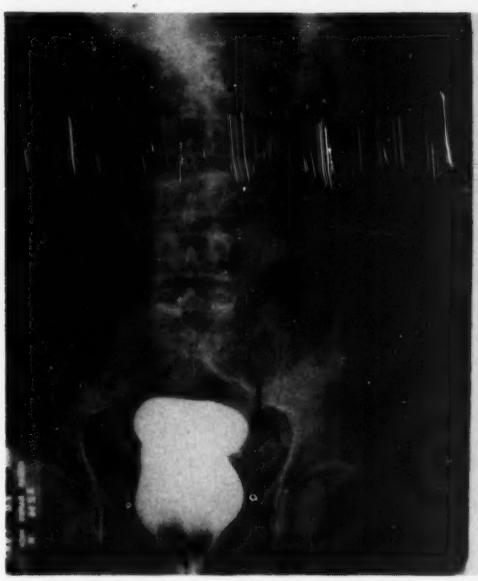


Fig. 7

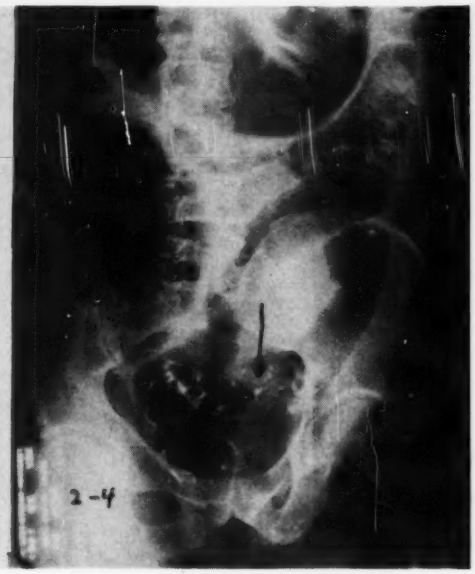


Fig. 8

Fig. 7—Case 2. Second examination. Practically complete obstruction at site of previous localized narrowing. Distention of proximal colon.

Fig. 8—Case 2. Second examination. Double contrast film reveals a short, very narrow, irregular channel and abrupt transition to a normal lumen on each side of the lesion. The proximal face of the lesion is doughnut-shaped.

had never been established. The patient had been feeling perfectly well and had not been having any abdominal cramping, weight loss, change in bowel habits, melena, or fresh bleeding with his bowel movements.

The patient was not apparently ill and although the abdomen was moderately distended the bowel sounds were normal. Proctosigmoidoscopic examination revealed a normal mucosa and lumen to the rectosigmoid at which level there was rather sharp narrowing of the lumen of the bowel but no evidence of intrinsic neoplasm. This finding suggested an inflammatory stricture of the type usually seen with diverticulitis.

Initial x-ray examination (Fig. 5) in this hospital in February, 1951 showed that a short segment in the mid-portion of the sigmoid colon was markedly narrowed, sufficiently to cause delay in the passage of barium. The area of constriction was moderately long (6 cm.) and that several diverticula were present in the involved area. Obviously this was a case of diverticulitis. But, as always in such cases, we look for areas of particular narrowing which may show enough difference from the pattern of the rest of the lesion to indicate a concomitant carcinoma. In the air injection film (Fig. 6) the major portion of the involved area was slightly distended by air, but a 1 cm. section remained extremely narrow with an irregular channel and an abrupt change to a more normal lumen at each end. Such variation in the pattern must be considered suggestive. The radiologic

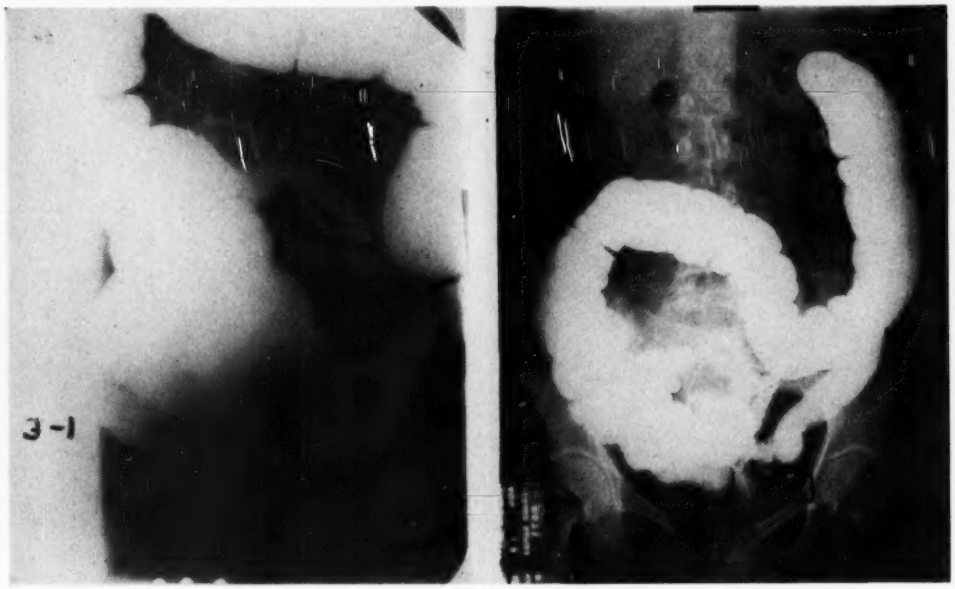


Fig. 9 Fig. 10

Fig. 9—Case 3. Initial examination. Localized diverticulitis of the sigmoid colon.
Fig. 10—Case 3. Postevacuation film of initial examination.

report concluded that an indeterminate situation was present and that there was need for a definite plan of further study, either microscopic or radiologic, as follows: "Marked localized constriction of the sigmoid colon. This may be on the basis of a diverticulitis. A small neoplasm cannot be ruled out, however, and resection should be considered unless a return to an adequate lumen can be demonstrated after a reasonable interval of medical therapy."

Medical management, to consist of hypertonic return irrigations and moderate dietary control followed by re-x-ray in two weeks, was recommended and the patient was discharged. He did not return as instructed, but came back in November, 1951 with an acute large bowel obstruction. Proctosigmoidoscopic

examination again showed sharp narrowing at the rectosigmoid without evidence of neoplasm.

After a lapse of ten months, considerable change in the radiologic appearance was expected. The barium filling film (Fig. 7) demonstrated a marked distention by gas of the proximal colon and of the small bowel, indicating mechanical obstruction of the distal colon. There was a practically complete retrograde obstruction demonstrated by the abrupt stop of the barium column in the mid-sigmoid. Beyond this point a very tiny trickle of barium had passed through an extremely narrow, short channel measuring two centimeters in length and a small amount had passed onto the proximal face of the obstruction to demon-

Fig. 11

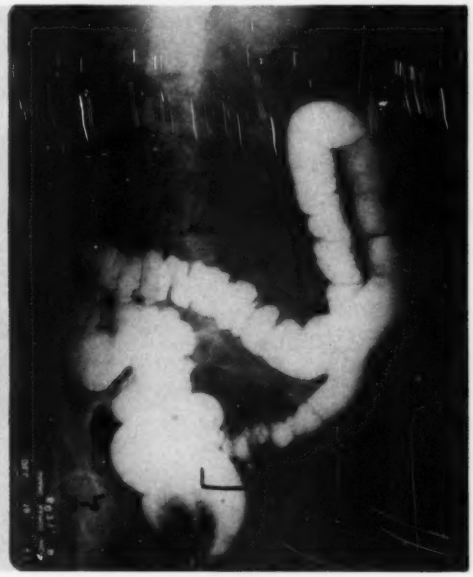


Fig. 12

Fig. 11—Case 3. Recheck 4 months later showing typical evidence of diverticulitis.

Fig. 12—Case 3. Recheck film demonstrating even distribution of the deformity without any localized variation in the pattern.

strate a doughnut-shaped proximal face of the lesion. This was also revealed by air injection films (Fig. 8) showing the short obstruction with abrupt termination at each end and with a symmetrical doughnut shape of the proximal face of the lesion. There was here no long drawn-out irregularity such as is usually seen with diverticulitis.

The etiologic diagnosis was still not proven but the radiologist concluded: "Complete obstruction of the mid-sigmoid. The lesion is probably a neoplasm but might be a localized recurrent diverticulitis. In either case resection is indicated".

Resection of the involved segment of bowel was done at this time and the patient's recovery was uneventful.

The surgical specimen was a segment of colon 11 cm. long, showing marked induration of the pericolic tissues in the middle third of the specimen; numerous diverticula were found throughout the length of the segment, some of these showing extreme edema of their walls, congestion and induration of the surrounding fat, and in one instance a tiny perforation. Some of these sacs contained fecaliths, but no definite abscess was found in the zone of maximum induration;

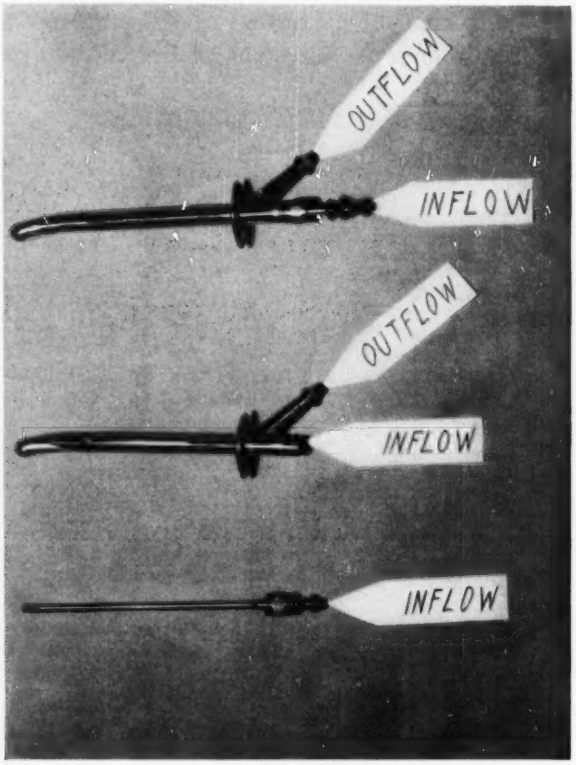


Fig. 13

Fig. 13—Return irrigator. At top—assembled. Middle—inner afferent channel, with spray tip. Bottom—outer sheath for unobstructed continuous return flow.

the bowel lumen had a caliber of only 15 mm. and the wall was rather rigid, with obvious hypertrophy of the muscle layers. There was no suggestion of neoplasia. Microscopic examination revealed considerable diverticulitis and peridiverticulitis with associated hypertrophy of the muscle coats proximal to the stenosed segment.

Differential diagnosis is not easy in these cases. Certainly the radiologic evidence in this second case is far more typical of neoplasm than in the first case which did have a neoplasm. Hedging by the radiologist in these situations is

not an attempt to avoid responsibility but rather to point out whatever lack of certainty may be present and the need for further action to reach a definitive diagnosis.

Case 3:–A sixty-four year old woman was seen in August of 1952. She was complaining of passage of bloody mucus from the rectum and a feeling of pressure in the rectum. There had been some weight loss of unknown degree. She had had abdominal soreness for about six months and five months previously had had a barium enema elsewhere which did not reveal any abnormality.

Abdominal examination was negative but proctosigmoidoscopic examination revealed a large amount of blood and mucus in the ampulla with marked narrowing at the rectosigmoid junction through which the scope could not be passed. No interruption of the mucosa was seen and it was the impression of the examiner that the patient had acute diverticulitis or that she had a neoplasm proximal to the range of the sigmoidoscope.

The initial x-ray examination in August (Figs. 9 and 10) showed the presence of many diverticula of the sigmoid colon with irritability of that area but without obstruction. The conclusion was "Diverticulitis of the sigmoid colon".

The patient was discharged to the care of her personal physician. It was recommended that she have a high protein, high carbohydrate, low fat diet and that she be given 250 mg. of terramycin four times daily for a ten day period. Dilute hydrochloric acid with each meal and daily hypertonic saline return irrigations were also recommended. A diagnosis of diverticulosis with deformity secondary to diverticulitis was made at that time.

When seen intermittently during the next four months the patient was doing well except for minor bouts of abdominal cramping and occasional rectal bleeding. There was no further weight loss. A barium enema for comparison with the original findings was ordered at the end of this period.

The follow-up x-ray examination (Figs. 11 and 12) again demonstrate a knot of diverticula in the mid-sigmoid area with marked irregularity involving an 8 cm. length of colon. No change was noted during the interval except that the length of the affected portion of the sigmoid was slightly increased. The radiologist commented in the report that "There is nothing about the appearance of this lesion to indicate malignancy." But he carefully qualified his conclusions by saying, "Marked localized diverticulosis and diverticulitis of the mid-sigmoid colon, unchanged during the past four months. Suggest resection of this area because of the likelihood of recurrent episodes of obstruction or partial obstruction and because it is impossible to rule out early neoplasm in such an area."

A statement that early neoplasm cannot be ruled out was not made because of the presence of any evidence suggesting malignancy. It was made to emphasize that when a major benign deformity is present a small malignant deformity may not be recognizable.

In the light of this x-ray report and due to the persistence of symptoms and of significant disability of the patient, a resection of the involved section of the bowel was done. At operation a sigmoid mass was found. There was no evidence of local or distant neoplastic involvement. The patient's recovery was uneventful.

The surgical specimen was a segment of colon 17 cm. long, at the distal end of which was a ragged ulcer 3.5 cm. long, involving most of the gut circumference; this lesion had an obviously neoplastic base, with visible extension of tumor into the subserosal fat tissue. No enlarged lymph nodes were found anywhere in the mesocolic wedge. Histologic examination revealed a well differentiated adenocarcinoma originating in the mucosa, and extending via the lymphatics into the subjacent muscle layers with commencing proliferation in the attachment of the mesocolon; moderate fibroplasia and considerable inflammatory reaction was present about the entire tumor mass. Numerous diverticula which were also present showed evidence of some chronic nonspecific inflammation of their walls and of the surrounding fat tissue, with very little activity apparent at this time, either grossly or microscopically; the cellulitis associated with the neoplasm had produced a rather extensive thickening and rigidity of the gut wall.

Discussion

These three cases have in common a problem of discovering neoplasm when diverticulitis is present. The first case was a very early neoplasm discovered almost fortuitously by x-ray recheck in an area of diverticulitis. The second was a case of diverticulitis presenting a false radiologic appearance of malignancy.

In the third case a carcinoma was completely hidden by deformity secondary to diverticulitis and was not suspected or found until the involved segment of bowel was removed and opened.

Some definite program of management must be followed in cases where major diverticulitis deformity is present in order to prevent diagnostic error.

The first step in management of such a patient is recognition of the fact that the deformity which is present due to diverticulitis wold prevent x-ray visualization of an early carcinoma in the same area.

The second step in management is to secure further x-ray study at a time of maximum remission of the inflammatory process. For this purpose the patient should be subjected to an intensive, brief course of medical therapy, the rational of which is directly analogous to the intensive medical therapy accorded to gastric and duodenal ulcers. This course of intensive medical treatment should not exceed a period of ten days or two weeks and should include every measure to cause subsidence of acute inflammation and secondary infection in the

diseased part of the bowel. In order to produce this result, we subject our patients to warm hypertonic saline return rectal irrigations twice daily, and for this purpose have developed a special instrument (Fig. 13). The spray tip directs the water against the wall of the colon in all directions. The open return channel prevents development of increase in intraluminal pressure. The rationale of irrigating these lesions with a warm hypertonic solution is identical to the rationale of irrigating and cleansing any infected wound, wherever it may be on the body and wherever it may be accessible. In addition to the mechanical cleaning effect of the return irrigations and the hygroscopic effect of the hypertonic solution, we use also one of the broad spectrum antibiotics in therapeutic doses over the same ten-day period of time.

If this plan of medical management is rigidly observed in a purely inflammatory lesion a repeat barium enema at the end of the ten-day period will usually show a marked regression of the defect in the bowel and a sufficiently good lumen throughout to permit the radiologist to rule out concomitant neoplasm.

If the deformity at the time of recheck is still enough to hide a carcinoma, then the management must proceed directly to the third step—segmental resection of the area involved. In most such cases there will also be some justification for resection because of partial obstruction, but it is important to remember that the resection is done because an area of uncertainty exists in the diagnosis. It is only by carrying out all three steps promptly when indicated that we can avoid missing an occasional carcinoma.

In inflammatory lesions of the bowel it is the impulse of the medical profession to put these patients on a so-called low residue diet which consists usually of a milk vehicle and includes various dietary elements having a low fiber and low spice content. This attitude toward a proper dietary control of inflammatory lesions of the colon is founded only on tradition. In all inflammatory lesions of the bowel including the series of cases now under consideration, we feel that the bowel does much better if supplied with natural and reasonable fuel, and from clinical experience, we know that all of these patients do better if they are put on high protein, high carbohydrate, moderately low fat diet which supplies normal bulk and from which milk has been entirely deleted. Milk not only contains tremendous allergenic potentialities but is a culture medium second to none; and though it may well be the most complete food per se, it does not provide proper bowel content.

AN INTEGRATED APPROACH TO THE MANAGEMENT OF CHRONIC ULCERATIVE COLITIS*†

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Chronic ulcerative colitis is a much discussed subject, yet one of which we know in reality very little. Recent research has clarified some aspects of this puzzling problem, and the time seems to have come to evolve a flexible treatment program adapted to the various stages of the disease and providing for coordination of the different specialties concerned in the management of chronic ulcerative colitis.

The syndrome may be defined as an idiopathic, or nonspecific inflammatory disease of the colon, characterized by successive phases of activity and quiescence, with frequent recurrences in spite of treatment. It affects subjects regardless of sex, age, or station of life, and has been reported as occurring in infants[1] and in juvenile patients[2].

Ulcerative colitis is unpredictable and variable as to extent of bowel involvement, its clinicopathologic course, and response to treatment. In 90-93 per cent of cases the rectum, beginning immediately above the mucocutaneous line is affected. The remaining 7-10 per cent of cases of ulcerative colitis manifest themselves by segmental distribution in the colon, occasionally reaching up to the distal ileum. McCready and his group[3] reported a higher incidence of ileal involvements, amounting to approximately 30 per cent. But even when the disease extends 4-5 cm. cephalad beyond the ileocecal valve, the signs and symptoms of ulcerative colitis are similar to those in cases limited to the colon.

Pathology and Etiology

On the basis of microscopic observations, Warren and Sommers[4] established two different types of nonspecific ulcerative colitis. Local vasculitis was demonstrated in 11 per cent of a series of 180 specimens, while crypt abscess occurred in 39 per cent, and the microscopic appearance remained indeterminate in fully one-half the number of cases. In local vasculitis the findings resembled periarteritis nodosa, and a similar group of changes was classified by Bargen[5] as thromboulcerative colitis.

A new concept of the pathogenesis of chronic ulcerative colitis has been proposed by Levine, Kirsner and Klotz[6]. Samples obtained during endoscopy showed alteration of the epithelial cells in the basement membrane, with the

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epithelium sloughing away, and subsequent formation of abscesses. This description corresponds to the second type of lesion, according to Warren and Sommers, but the change is traced by Levine and his associates to collagen disease.

Chronic ulcerative colitis was ascribed by Dragstedt, Dack and Kirsner[7] to *Bacterium necrophorum*, which they were able to isolate in 70 per cent of a series of 298 patients. As the organism is probably present in the normal alimentary tract, an additional factor must be assumed which causes the bacteria to multiply and produce necrosis of the mucous membrane of the bowel. It has been suggested that *Bacterium necrophorum* is merely a secondary invader. The same argument applies apparently also to the role of diplostreptococcus in the streptococcal type of ulcerative colitis, but it is nevertheless imperative to eliminate all possible foci of infection, especially to remove infected tonsils and teeth, and to control sinusitis.

Lysozyme is not the cause of chronic ulcerative colitis, but rather its result, and the titer of this mucolytic enzyme may serve as an index of the degree of activity of the ulcerative process[8]. Lysozyme inhibitors[9] such as dioctyl sodium sulfosuccinate have proved ineffective to change the course of the disease, or to produce a remission.

The role of upper respiratory infections as a predisposing factor to onset and recurrences of the disease has been stressed by Bargen, Jackman and Kerr[10].

This brief review of recent pathologic, microorganismal and enzymatic research shows that the nature and cause of chronic ulcerative colitis still remain doubtful, and attention has been increasingly focused upon the psychogenesis of this serious disease. While the etiologic significance of psychiatric factors is nowadays almost commonly accepted, the controversy centers mainly about the question whether situations of emotional conflict are the true cause of ulcerative colitis or merely precipitate exacerbations and recurrences[11]. At a time when emotional conflicts are the number one problem in medicine, this fine point should not be too much stressed, and a clear understanding of the type of personality structure and emotional crisis which predispose to ulcerative colitis is required.

Environmental situations charged with anxiety, fear, frustration, excitement, hostility and resentment leave their telltale scars along the gastrointestinal tract. Life's every-day stress and strain taxes the emotional stability of each individual. The "termites" of worry, maladjustment and nervous exhaustion have consumed the foundations of many a sound constitution. This trend in modern civilization is marked by the fact that the fifth most common cause of death under fifty years of age is suicide.

The effect of emotional stress on the gastrointestinal tract has been most extensively studied in the series of publications by Stewart Wolf, Harold G.

Wolff, and their co-workers at Cornell University Medical College[12]. Adverse life situations stimulate gastrointestinal activity to such a degree as to initiate morbid processes predisposing to the breakdown of the gastrointestinal mucosa. At first, emotional upsets produce only a transitory effect, but repeated and prolonged disturbances may result in the definite clinical syndrome of idiopathic ulcerative colitis. Sustained stimulation of the gastrointestinal tract manifests itself by engorgement, increased production of mucus, and hypermotility with subsequent diarrhea. Finally there develop miliary, pinpoint ulcerations which later on become superimposed with abscesses. The pathologic process, slow and reversible in its early phases, is accelerated as time goes on, and rapidly reaches the stage of a permanent lesion.

Emotional problems were discovered in two-thirds of the patients attending the Clinic for Digestive Disorders at White Memorial Hospital. Symptoms of nervous indigestion, abdominal discomfort, nausea, vomiting and diarrhea occurred frequently in neurotic or abnormally sensitive individuals. When their emotional problems were resolved, these symptoms suddenly disappeared.

The fully developed syndrome of chronic ulcerative colitis presents a picture of such complexity that it is well-nigh impossible to determine the etiologic factors responsible, but in the vast majority of cases the common denominator is a disordered emotional life. Once this fact has been recognized, timely diagnosis of ulcerative colitis by proctoscopic examination can lead to appropriate management.

The proctologist will undoubtedly identify the mucosal changes characteristic of chronic ulcerative colitis; but it may be useful to review the peculiarities of the personality structure of patients suffering from this disease, as determned by Groen[13]. They are of keen intellect, dress carefully and neatly, and are in every respect accurate and conscientious. They are extremely sensitive and often display a hesitating, unbalanced attitude toward the value of their own personality; such patients are markedly egocentric, and generally have a passive attitude. Fear is a dominant feature, and faced with a challenge they prefer to retreat, exhibiting a striking lack of aggressive drives. Their need for love, sympathy and affection is great, but as they are emotionally immature their concept of love is sentimental, naive, and infantile. Male patients show an abnormal fixation on their mother, combined with fear of their father, while females are equally attached to their father, but exhibit aversion against their mother. In the beginning they will deny the existence of an emotional conflict and its connection with physical disease. Turell, Krakauer and Maynard[14] stress the significance of insecurity during childhood. According to White[15], subjects with ulcerative colitis are upset by the kind of environmental situations which would hardly be registered as calamities by well balanced persons. In our own observations we found that such patients are apt to develop symptoms only after their sheltered life has been disturbed and their wishes and desires frustrated. In the choice

between two evils they choose both. If employed, they have their work on their mind instead of keeping their mind on their work.

Diagnosis

In ulcerative colitis, the rectum and colon present a characteristic picture. Sigmoidscopy readily discloses the various stages of the disease. Early changes include primary inflammation, edema, and typical granular appearance of the mucosa. In the chronic phase the bowel wall loses its elasticity, becomes ulcerated, and there may be strictures and signs of pseudopolyposis. Roentgenograms of the colon, using barium as a contrast medium, will not only confirm the sigmoidoscopic findings, but also determine the extent of involvement.

In the differential diagnosis of segmental ulcerative colitis such diseases as diverticulitis, carcinoma, syphilis, tuberculosis, actinomycosis, and the dysenteries must be taken into consideration. Carcinoma, however, is superimposed upon chronic ulcerative colitis in approximately 1-3 per cent of cases. The average duration of symptoms of ulcerative colitis prior to discovery of carcinoma is ten years, and a high grade of malignancy with rapid invasion of surrounding structures is the rule[16].

Complications

Within the bowel, chronic ulcerative colitis may be complicated by hemorrhage, perforation, obstruction, malignant processes, or anal incontinence, often accompanied by development of a fistula. Regional ileitis is observed in 30 per cent of cases. Allergic sensitization of the colonic mucosa is a very important clinical factor in the course of ulcerative colitis.

Outside of the bowel, chronic ulcerative colitis may be complicated by rectovaginal fistula, periurethral invasion, skin eruptions of the necrotic type, palpable spleen, reversible clubbing of fingers, or amenorrhea. In cases of long standing, cirrhosis of the liver is apt to develop, or again renal calculi may appear due to lack of motion and prolonged dehydration. Occasionally, loss of sodium, potassium, and chloride, sufficient to cause shock, is observed. About 10 per cent of cases are complicated by arthritis, which especially in young adults precedes bowel symptoms. Chronic ulcerative colitis may also be accompanied by rheumatic eye disease, sometimes terminating in blindness.

Pregnancy complicating ulcerative colitis leads almost invariably to an exacerbation of the disease. Still less favorable is acute onset of ulcerative colitis during pregnancy or puerperium. Previous ulcerative colitis, quiescent at onset of pregnancy, is reactivated only in about one-third of the cases[17]. Thus it would seem advisable to postpone pregnancy until a long time has passed since the last attack. Therapeutic abortion on account of concomitant ulcerative colitis is not indicated, as the course of disease is hardly ever improved by such an intervention.

Medical Management

Treatment of chronic ulcerative colitis with antibiotics has proved generally disappointing. Many patients are unable to tolerate aureomycin, terramycin, erythromycin, and similar antibiotic agents. These substances apparently irritate the mucosa and result in nausea, vomiting and diarrhea, the latter usually due to membraneous colitis associated with a mycotic type of pruritus ani. Antibiotic agents destroy the beneficial bacteria along with the harmful ones, and at the same time decrease the ability of the bowel to resist further invasion. The primary pathologic process is not controlled, but merely masked. Transient symptomatic improvement will therefore only serve to interfere with a real understanding of the disease and its progress.

Chemotherapy is of limited usefulness. Sulfadiazine or its conjugated form, acetylsulfapyradine (Azulfidin) has proved successful when used together with other supportive measures. Sulfaguanidine also gives promising results, but has now been replaced by neomycin combined with sulfathalidine. In the presence of fever, sulfadiazine, alone or with other medication, is the drug of choice.

Pro-banthine, an anticholinergic agent, affords subjective relief. Especially when the drug is used in conjunction with metamucil, gastrointestinal activity is inhibited, and such rest may result in encouraging objective improvement.

Corticotropin (ACTH) and cortisone exert no curative effect on ulcerative colitis, but merely induce remissions without affecting the underlying pathologic process. These hormonal agents, nevertheless, are helpful in tiding the patient over a critical period, thus permitting preparation for surgical intervention. Hormone therapy often leads to dramatic reactions—especially a feeling of well being, improved appetite, and increase in weight. A trial of hormonal therapy is indicated whenever ulcerative colitis is accompanied by arthritis of the rheumatoid type. But in prescribing ACTH or cortisone one must always keep in mind that there is a possible danger of perforation of the gut in the ulcerated area or at other sites. It must furthermore be remembered that relapses are frequent following termination of hormone therapy[18]. In spite of temporary subjective improvement no lasting change in the patient's personality structure can be expected from medication alone.

Prescription of vitamins assumes importance as supplementary therapy. Vitamin A, administered parenterally in doses of 50,000 units every three or four days, reduces atrophy of the epithelial cells and thus lessens the fragility of the mucous membrane. Rucon, a product combining rutin with Vitamin C and calcium phosphate, inhibits bleeding in mild cases. Mutiple vitamin deficiencies (A, B_1, B_2, and possibly D) resulted in almost two-thirds of Mackie's[19] cases in such clinically recognizable lesions as glossitis of nicotinic acid deficiency, cheilosis and seborrhea of the naso-labial skin, due to ariboflavinosis, and the dry, hyperkeratotic skin of Vitamin A deficiency.

Nutritional deficiencies are a secondary phenomenon of chronic ulcerative colitis, but often the chief clinical problem. Among the more frequently encountered deficiencies are hypoproteinemia, sometimes to the extent of edema; disturbances of calcium and phosphorus metabolism, occasionally even resulting in tetany and osteomalacia; hypochromic microcytic anemias, due to iron deficiency; and—less frequently—macrocytic anemias. The diet is planned to compensate for specific nutritional deficiencies; in general it should be of high caloric content, with large amounts of protein, and designed to control electrolytic imbalance of potassium, sodium, and chloride. In severely toxic cases transfusions have proved to be an excellent supportive measure.

Relaxation of the hyperactive colon is achieved through antispasmodics. Yet it is not sufficient to bring relief from tension to the affected organ alone, and the patient as a whole must learn to lead a more restful life. Sedation is likely to result in temporary improvement, but more enduring effects can be expected only from psychotherapy.

Psychotherapy

The psychotherapeutic measures required are merely of the supportive type and do not call for referral of the patient to a psychiatrist. Indeed the attending physician or the nurse are best suited to give encouragement and reassurance. In view of the psychological immaturity of the typical patient with chronic ulcerative colitis, it has been suggested that the physician should think of him as of a child and be prepared to assume the role of a parental figure[20]. But this is only the starting point in helping the patient to a better adjustment to the situations which brought on the crisis. Whenever a subject with chronic ulcerative colitis is referred to us for consultation, he receives complete attention and is permitted to discharge his emotions, aggressive feelings, and inadequate efforts to cope with life's stress and strain. No medication known to man can replace the truly sympathetic and understanding attitude of the physician who prompts the patient to reassert himself and to change from an attitude of despair to one of challenge.

Chronic ulcerative colitis must be regarded as a manifestation of a feeling of inadequacy which—if not relieved—will persist, waiting only to be rekindled by the next emotional upheaval. Every psychosomatic illness constitutes a vicious circle: in the maladjusted, personality complexes produce stress and tension which act upon the susceptible organ to cause or aggravate the disease; the resulting symptoms, in turn, will intensify the environmental difficulties.

It is necessary to break this chain of events at some point. Whenever medical management combined with psychotherapy fails to bring on an improvement, surgical intervention must be taken into consideration. White[15] reported that ileostomy alone or combined with partial or total colectomy resulted in a series of 13 patients in complete remission of all complaints of ulcerative colitis; the symptoms of depression, negativism, and petulance disappeared following

surgical intervention, while the dynamic psychologic factors of immaturity, dependency, and hostility remained unimproved.

Indications for Surgery

In addition to this psychiatric indication, a number of others have been established on the basis of clinical conditions and sigmoidoscopic findings. Lahey[21] recommended surgical intervention in acute exacerbations of ulcerative colitis which fail to respond to ACTH; when the disease is complicated by hemorrhage with the danger of impending shock; in the presence of acute and chronic perforation; whenever intestinal obstruction occurs; furthermore, following development of multiple anal fistulae and rigid anal sphincters; finally, when colitis is complicated by joint involvement.

Other conditions in which operation should be seriously considered include: fulminating progressive diarrhea; recurring or persistent pseudopolyposis; dehydration and toxemia with impending shock; chronic debility, anemia, toxemia, cachexia, arthritis, thromboembolic disease, liver degeneration, and kidney involvement. It still remains an open question whether malignant disease shows a predilection for the site of nonspecific ulcerative colitis. But the clinical signs of early carcinoma are identical with those of chronic ulcerative colitis, and surgical intervention should be performed whenever there is the slightest suspicion in the diagnostician's mind.

Ripstein and his associates[22] recommended radical primary resection of the colon, combined with ileostomy in patients with permanent organic bowel changes, or in the presence of complications. Resection of the colon stops the loss of protein (estimated at 100-200 mg./24 hrs.) and of blood 100-300 c.c./24 hrs.). At the same time absorption of toxins, occurring particularly in the ascending colon, is controlled.

In moribund patients, ileostomy is indicated as an emergency operation. Otherwise the intervention should be carried out as an elective procedure, to be scheduled following due preoperative preparation, and after the patient has become an acceptable surgical risk. Improved preoperative and postoperative management has rendered even radical colon resection relatively safe, and ileostomy alone is no longer considered an adequate measure. An exception is segmental ulcerative colitis, in which the hazard of spread is much reduced. This type responds well to segmental resection, provided that 12 inches of healthy colon are excised on either side of the line of demarcation.

This is not the place to enter into a discussion of the various surgical procedures, but it is important to remember that the technic of ileostomy, alone or combined with more extensive resections, has been so much improved that the rate of mortality and morbidity is greatly reduced. Through the introduction of ileostomy bags, cemented to the skin, postoperative complications have been largely eliminated, and it is made easier for the patient to adjust to his disa-

bility. Nowadays it has become popular for ileostomy patients to form clubs in which they exchange information regarding the proper management of their handicap, and otherwise help each other to face life with a balanced mind, and free from depressions. In a recent series, more than 86 per cent of patients were successfully rehabilitated following discharge from the hospital[23]. All these facts are important in weighing the advisability of surgical intervention. When physicians and other medical workers can explain to their patients how simple and easy the postoperative management has become, there will be less objections to the operation.

The decision as to what constitutes the medical phase of ulcerative colitis, and at which point surgical intervention becomes advisable should be reached in consultation among the various specialists concerned. Team work between the internist, gastroenterologist and proctologist, assisted in selected cases by a psychiatrist, is the key to successful management of ulcerative colitis. There is always the danger that medical management is continued until the patient goes into shock. On the other hand, failing response to various other types of medication and therapy does not in itself constitute an indication for surgical intervention. In some patients the operation may prove mechanically successful but still fails to contribute to their emotional stability.

In this team of specialists, the proctologist plays an important part. Ulcerative colitis starts almost invariably in the rectum, and the proctologist is thus likely to be the first one consulted. Even in the presence of nonspecific symptoms he will immediately think of ulcerative colitis. Familiar with the early signs of the disease, he can evaluate the sigmoidoscopic findings, arrive at a prompt diagnosis, and suggest appropriate therapy. On the strength of his experience, the proctologist is best able to evaluate the patient's emotional instability and immaturity, and should always be consulted to determine whether surgical intervention is indicated, and at which stage it holds out the greatest promise of optimal results. While thus the management of chronic ulcerative colitis calls for the team work of various specialists, the proctologist should serve to integrate and direct the coordinated efforts.

Summary

1. Chronic ulcerative colitis is reviewed as to pathology and etiology, with special attention to its psychosomatic component.

2. The diagnosis of the disease and its principal complications are briefly presented.

3. Means and limitations of medical management of chronic ulcerative colitis are discussed.

4. Psychotherapeutic measures are a valuable adjunct in the management of chronic ulcerative colitis.

5. The specific indications for surgical intervention are enumerated, and the need for rehabilitation following ileostomy is stressed.

6. Successful management, whether medical or surgical, calls for the team work between internist, gastroenterologist, and proctologist; it is up to the latter to coordinate the various specialized procedures and to integrate them into a comprehensive treatment program.

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OBSERVATION OF THE BENEFICIAL EFFECT OF SPRUE DIET ON ULCERATIVE COLITIS

Preliminary Report

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The approach to the treatment of chronic ulcerative colitis is encumbered with so many disappointments and controversial opinions, none too hopeful, that the observations derived in this paper are presented very humbly with fervent hope that this type of management will open a new avenue to an ultimate conquest of this dreadful disease. The conclusions reached in our study embrace a period of the past three years. When a number of our chronic ulcerative colitis patients had relapses, in desperation when all of the established methods of therapy, such as, terramycin, sulfa, ACTH and cortisone, failed, a modified sprue diet was instituted. The improvement was dramatic and it followed from 48 hours to 4 days after starting the specific diet.

The principle of this diet is restriction of carbohydrates other than that found in fruits or in some vegetables and permitting only protein milk. Sugar is strictly prohibited and any products containing sugar must be diligently avoided. Potato and any cereal grain, such as, corn, rice, wheat, rye, are strictly prohibited. Canned vegetables occasionally contain sugar and must be avoided. Neutral fats, such as, yogurt, sour cream, non-salty butter in small amounts are tolerated. Eggs are permitted and should be used only when the diarrhea abates a little. Cottage cheese (non-salty), cream cheese (in small quantities) are permitted. Lean meats and fish are permitted; gelatin is advisable; honey is tolerated. In addition—all food must be pureed—100 mg. of thiamine and 15 micrograms of rubramin are given daily hypodermically for about 30 days.

At the start, for one week, the patients get only cottage cheese, lean chicken, veal, sweetbreads, oysters, filet of flounder, pike, perch, bananas (excellent) and protein milk. After a week or so, we add orange juice sweetened with honey and gelatin, and an egg. Then, various vegetables are gradually augmented being careful to add the items one at a time. For instance, first we introduce carrots into the diet; if it is well tolerated, then squash, etc. Some vegetables may start a recurrence of diarrhea so at this point one has to be very careful and withdraw the offending vegetable for a time.

This type of diet is continued for at least three months and then carbohydrates, such as, potatos and bread are added. The quick response to this regimen was so gratifying that each time we started this diet on an obstinate case, feeling that this time it may fail, we were pleasantly surprised that it was successful in each instance.

The cases selected were only of the most obstinate form with extensive ulcerations, with profuse bleeding and roentgenological changes. Few of the cases in our series are quoted because of the length of their colitis and resistance to all forms of treatment.

Case 1:—Mrs. R. G. 38 years old, white female, stated that since childhood she had frequent bowel movements. In 1934 she was diagnosed as having ulcerative colitis. She spent 8 months at Walter Reed Hospital with slight improvement. She came under our observation in 1946. We treated her with established regimen for a period of three years, with indifferent results. We then suggested that she see a colleague of ours, feeling perhaps that psychologically a new broom would sweep better. After one year she returned to us at which time we were interested in treating various diarrheas with modified sprue diet. Her response to that diet was immediate and sustained. She gained weight, the number of her bowel movements diminished and the proctoscopic and roentgenological pictures showed definite improvement.

Case 2:—Mrs. J. R. D., daughter of a physician, age 29, had ulcerative colitis since childhood. She came to see us in 1950. She was extremely emaciated, anemic, with extensive roentgenological changes in her bowels, proctoscopically an easily traumatized mucosa, bleeding profusely, spastic and granular. Her response to the diet was immediate and sustained. Six months later a polyp was found proctoscopically on a normal mucosa. The x-ray showed a microcolon and her bowels were free of blood. An interesting thing about her was that in the interim she went through a pregnancy last year without any adverse effect on her colitis or her baby!

Case 3:—Mrs. A. G., 30 years old, white female, with a history of ulcerative colitis of fifteen years' duration. For the past four years the diarrhea and blood were continuous. She had 20 b.m. per day. We saw her May 1953. Her response was immediate and at present writing there is no blood in her stools and she only has 7 formed small stools daily without tenesmus.

Comment:—One cannot help to speculate, being familiar with ulcerative colitis, that there must be a metabolic factor which acts as a trigger mechanism starting it. The role of the pancreas has not been often emphasized and one wonders whether or not it is the *casus mali* in initiation of the disease. The satisfactory response of obstinate cases of ulcerative colitis to the modified sprue diet makes us inclined to think so.

Summary:—Improvement in advanced ulcerative colitis followed a modified sprue diet.

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INTRAMURAL ABSCESS OF THE COLON WALL IN CHRONIC ULCERATIVE COLITIS

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In the chronic type of ulcerative colitis complications are numerous in kind and incidence. In ileitis, perforations and sequential sinus formations are more commonly met with than are like conditions in the colon in which sinus formation is more rare. This difference in ulcerative colitis is probably due to the gradual development of a barrier of fibrous tissue that prevents penetration through the wall of the colon. As a rule, when perforation of the colon takes place, peritonitis ensues. Abscesses and fistula formation, however, are seen more often in the rectum and sigmoid. These abscesses usually drain into the rectum or outside the anus with fistula formation; the incidence of perirectal or lower colon abscess is relatively high. What may be termed intramural abscesses must be exceedingly scarce because such lesions receive no mention in the literature on ulcerative colitis. Two such cases have been met by me, and since they caused an alarming state of illness, and each had some special clinical features, they seem worthy of recording. The two cases presented such similarities that the description of one could answer for the other one.

A young woman of 24 years was first seen in December 1946. The family history had no instances of insanity, but all the members were of a neurotic and nervous type. The past history of the patient was not relevant, excepting that she was never strong and had had many minor illnesses. For the seven months previous, she had been suffering from abdominal cramps and diarrhea, the movements increasing, at the time she was seen being about ten a day and fluid in character. There was considerable nausea; anorexia was pronounced. She had lost 50 pounds in weight since the illness began, which started when she was grieving about the loss of her father and worrying about the upset in her home.

The examination presented a poorly developed young adult of 80 lbs.; having a moderate hypochromic anemia; pulse 96; temperature 99.8°F.; a dilated and ptosed stomach and colon. The rectal mucosa was deeply congested and bled easily. The urine was high in indican, and the stool fluid, fetid, containing free blood, and a high Welch bacillus, parasitic E. coli and an above normal content of hemolytic streptococci. The deductions from the x-ray examination were marked spasm in the stomach; transit through small and large intestine rapid; marked spasm and rugae pattern changes in the colon (descending and transverse).

Medical treatments were established which consisted of replacement electrolyte injections, a few regularly given small (250 c.c.) blood transfusions, intravenous mercurochrome, bismuth by mouth, high protein diet, supplemental

feedings, rest, heat to abdomen and autogenous coli and streptococci vaccine. On these she benefited slowly. Before this treatment was instituted, she had been on sulfa drugs, penicillin and streptomycin without benefit. In the course of a few months she was markedly improved, had one or two semi-solid and some solid bowel movements a day, and came up to 125 lbs. in weight. In the third year afterward, the patient gave birth to a normal baby and, other than an occasional anemia and furuncles, continued in reasonable health. Several x-ray examinations showed a constantly present typical picture of a smooth fibrotic type of colon. The rectal mucosa continued to look reasonably healthy. Thus we have here a case of ulcerative colitis that, under medical treatment, improved and remained in fairly satisfactory health for several years.

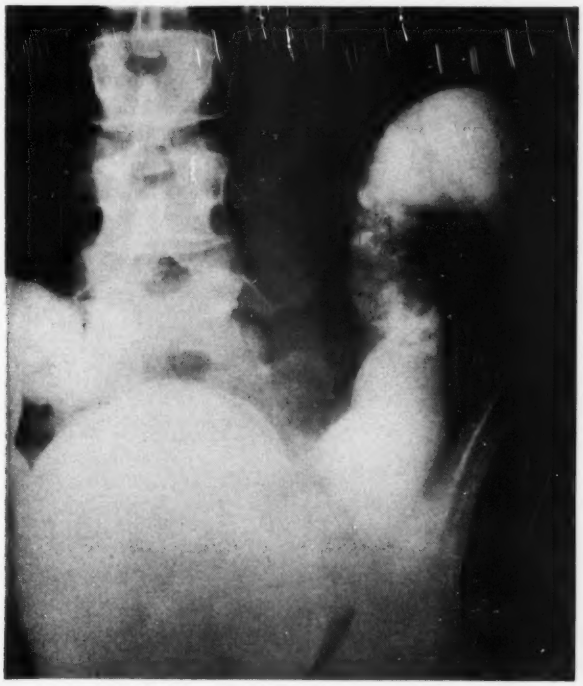

Fig. 1—Showing pointing up and stoppage of barium by rectum at distal end of the tumor mass.

In the early part of 1952, seven years after the beginning of treatment for the ulcerative colitis, she began to run short bouts of fever, lasting for a few hours and then perhaps not present for days at a time. She lost weight steadily; became ill-looking; at times her pulse was moderately elevated; the temperature at office visits not being higher than a degree or two on any of several visits. Her erythrocytes dropped to 3,900,000 and hemoglobin from 87 to 61 per cent; white cell count going to 14,000 with 79 per cent polys.

A mass in the left upper abdomen became more noticeable, which at first was not tender, but in a few weeks became definitely so on pressure. Beginning

about two weeks before she was operated upon, she suffered acutely at times from subjective pain in the upper and left abdomen.

The x-rays taken at the time showed the typical picture of ulcerative colitis. The colon was smooth without any haustra or mucosal pattern, with several contracted areas, but no definitive obstruction was present. Incidentally, her bowels had moved about twice a day throughout this last illness, the movements remaining semi-solid with no blood. On the fluoroscopic examination, compression obliteration of the involved area was not possible, and a diagnosis of malignant disease associated with ulcerative colitis was suggested. Clinically, however, the type of illness and the other findings considered, the case was judged as one of an infective illness and the diagnosis of intramural bowel

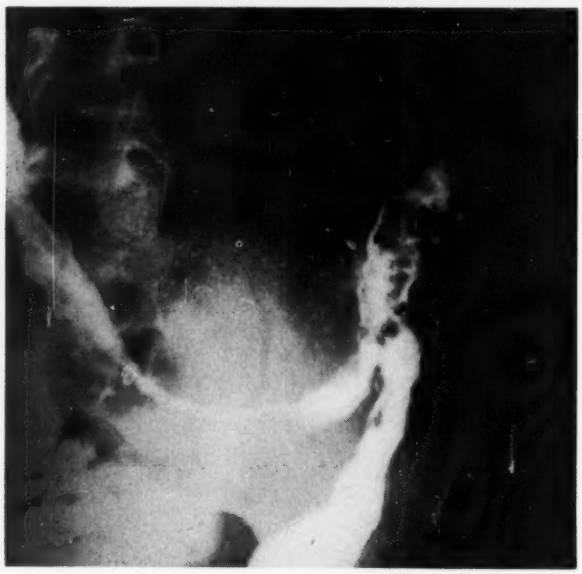

Fig. 2—Showing the area of tumor formation (transverse portion). There were no clinical signs of intestinal obstruction. Barium by mouth.

abscess was made. The tissue examination is as follows:— "The segment of bowel measures 36 cm. in length and its average circumference is 5.7 cm. proximally and 4.5 cm. distally. The mid-portion has a large tumefaction extending into and involving the mesentery. The serosal surface is deeply injected, has some hemorrhages and is covered with a fibrino-purulent exudate. The wall feels edematous and one portion has sensation of fluctuation. The wall of the entire colon feels thick and edematous. On opening it is filled with hemorrhagic and purulent contents. In the mid-portion, corresponding to the tumefaction, there is a perforation extending from the mucosa deep into the bulge involving the mesentery. The edges are raised, soft, nodular, somewhat yellowish in color and the cut surface has a great deal of silvery-white firm tissue, the consistence of a rather cellular malignant mass. The entire intestine proximal to the perfora-

tion is nodular, soft, has a completely distorted mucosal pattern and has several shallow ulcers. One section has a series of abscesses which lie in or close to the submucosa. They extend practically to the upper resected border. Distally, the pattern is quite similar. There is considerably less edema, the intramural abscesses are considerably less abundant and confined to the area close to the large perforation. The wall is somewhat firmer and there are numerous shallow firm ulcerations.

"*Microscopy:*—The features common to all portions of the intestine are marked edema, more or less infiltration by lymphocytes, plasma cells and eosinophilia, the presence of large lymphoid nests and lymphoid follicles situated intramurally, a submucosal fibrosis and a fibrino-purulent exudate on the serosa. At the point of perforation the entire wall is destroyed by an acute necrotic process which leads down into a large abscess cavity involving the mesentery. There is tremendous edema, intense engorgement and numerous young venous thrombi.

Fig. 3—Section of tumor formation showing thickening of the colon with several of the small abscess formations (dark areas). Of these there were about twenty. Penetration of mucosa not showing. Mucosa below showing many pseudo polyps.

In the intestine, proximal to this area, the edema of the wall is very marked, the lymphoid follicle formation is present in submucosa, muscle and subserosa. There is a dense diffuse, mixed inflammatory reaction, with numerous acute ulcers of the mucosa and very many intramural abscesses. The latter are situated in the submucosa, in the muscle and in the subserosa. The mucosa at the edges of the ulcerations is extremely edematous. In some of the acute areas there is a polypoid granulation tissue projecting above the preserved mucosa. Distal to the large abscess the scarring of the wall is more evident and the edema is much less marked. The diffuse infiltration of lymphoid cells, plasma cells and eosinophils is greater close to the acute perforation and diminishes toward the distal resected edge. There are a few shallow ulcers close to the perforation, the remainder of the mucosa being free of ulcer but having innumerable polypoid masses covered by normal epithelium. The submucosa here is densely scarred and very thick".

After the excision a double barrelled colostomy was made which was broken down by clamp on the fifth week and the patient made an uneventful recovery with a rapid resumption of health.

The cases presented the following, which seem to be useful for diagnosis: The presence of a chronic ulcerative colitis, even though the case has been controlled in character for years, the number of movements few, and the general health reasonably satisfactory. The illness is of a mild and irregular febrile type, the temperature being variable, so that it may not be present for days at a time. A mass is present somewhere along the course of the transverse colon, and this is tender to pressure, and makes one suspicious of malignant formation.

During the course of the infection in the colon wall there is no definite change from normal in the white blood cell count. There is a short penetration formation stopping well within the bowel wall. This leads into a large abscess and a number of small abscesses with patches and areas of suppuration here and there along several inches of the colon. The peritoneum is intact and without inflammatory involvement.

The tissue of both cases showed definite pathology of ulcerative colitis even though several years had passed of reasonably good health, and no suggestion that the ulcerative colitis was worse or in a remission. In neither one was the bowel wall obstructed, and in both no x-ray suggestion of the lesion was observed. The swelling of the bowel wall bulged outward and not into the lumen.

Both cases did well on excision of the colon, and a double barrelled colostomy which was closed in a few weeks time.

Conclusion

Intramural abscesses of the colon above the sigmoid must be considered a complication of chronic ulcerative colitis. The process causes serious acute illness without perforation into the general peritoneal cavity until perhaps very late, and is easy enough to diagnose and not be confused with carcinoma if the symptoms are kept in mind.

EVALUATION OF CLINICAL METHODS IN GASTROINTESTINAL DISEASE

VI. New Approach to Antiulcer Therapy: Organic Potassium Salts (F111) and Ox-bile Products in Patients with Simple Duodenal Ulcer:*

Preliminary Report

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Peptic ulcer is an extremely common disease. It is an affection encountered in both civilian and military life, yet its pathogenesis is still problematic. Quite a large percentage of ulcers treated medically and some even surgically may recur, proving that neither treatment is wholly satisfactory.

There is no definite etiological factor known today for the cause of peptic ulcer. The vascular, neurogenic, chemical, spasmogenic, catarrhal, stress, and constitutional factors may be mentioned. Recently there has been a renaissance of the neurogenic[1] and spasmogenic[2] theories, with increased evidence of emotional and mental conflicts. They fail, for instance, to interpret why only certain individuals are afflicted with peptic ulcer. They do not explain why the affection is prevalent in certain countries and not in others; nor why it occurs in some races more frequently than others. Of all the evidence presented to uphold the various theories of the cause of peptic ulcer, the author believes the most acceptable is that supporting the role of the constitutional factor[3].

General Treatment

There is at present no specific medical treatment for peptic ulcer, certainly none based directly on pathogenesis and etiology. The purpose of medical therapy[4] is to reduce gastric secretion, spasm, motility, and mental unrest. The types of therapy may be divided into dietary and medicinal. The former consists mostly of milk, fruit juices, and carbohydrates which reduce secretion and dilute acidity. Drugs of the absorbable alkalis such as bicarbonate, magnesia, and calcium have been replaced by the nonabsorbable alkalis such as aluminum hydroxide gel, syntrogen, gelusil, etc. These alkalis buffer acid and reduce peptic activity and stimulate mucin. They act by absorption, neutralization, and astringency. Antispasmodics in the form of atropine lessen acid secretion and diminish excessive tone. Resin (anion exchange) absorbs pepsin and hydrochloric acid in the stomach and transforms it into an alkaline environment of

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*The organic potassium salts (F111) and ox-bile powder medications were generously supplied by Arlington-Funk Laboratories, Division of U. S. Vitamin Corporation, New York, N. Y.

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the intestinal tract[5]. Anticholinergic drugs act through their ability to inhibit the transmission of neural stimuli at the sites where acetylcholine serves to transmit the impulse. Recent drugs such as methantheline bromide or banthine bromide, pro-banthine[6] and prantal methyl sulfate[7] have been extensively used. Since the mucolytic enzyme lysozyme is found in high concentration in areas where ulcers are most frequently found, some believe it may be a predisposing factor. Such an antilysozyme substance sodium lauryl sulfate has been utilized clinically in the preparation kolantyl[8] with questionable results.

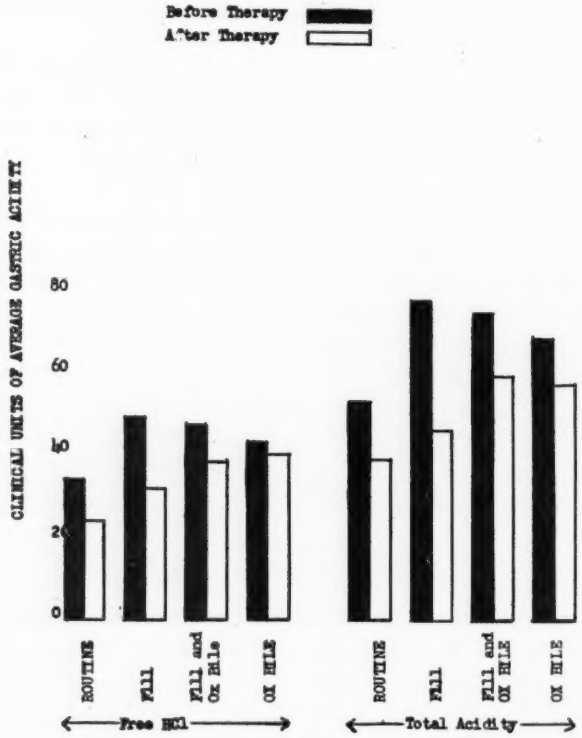

Fig. 1—Graphic representation of arithmetic mean values of free and total acidity in duodenal ulcer patients before and after varied therapy.

Recent publications of the newer anticholinergic drugs mention a wide variation among individuals in the degree of secretory inhibition and in the occurrence of side-effects with the same dose of an anticholinergic drug. None of the compounds produce the desired degree of secretory inhibition consistently[9].

Casimir Funk and his associates[10] using Shay rats as test animals for the ulcer problem have attempted to isolate enterogastrone or urogastrone. They obtained from the mucosa an active fraction which proved to be potassium acid acetate. They studied the preventive action of certain salts of organic acids on the formation of stomach and esophageal ulcers in the Shay rat. Potassium acid

acetate displayed a marked curative and preventive action by its effect upon salt water metabolism, acidity, and ulceration. The stomachs of treated animals are coated with a mucus-like lining. Potassium acid acetate has a pH value of 4.5 while the usual antiulcer preparations exhibit an alkaline reaction. In potassium deficiency in dogs, there is an increase in water exchange and volume of gastric secretions[11]. Funk and his co-workers[12] further noted that Shay rats showing evidence of hematuria or highly pigmented urines were relatively resistant to ulcer production. Bile and some of the bile acids proved to be effective antiulcer agents in Shay rats. This suggested to them[13] that bile may act as an antiulcer agent. Bile compounds reduce secretion of acid rather than to neutralize acid that is normally secreted. In the Shay rat no synergistic action between potassium acid acetate and bile therapy could be detected.

Since the present antiulcer medications are of no definite significant benefit with varying results and expense, it was attempted to utilize the present drugs, organic potassium salts (F111) and ox-bile as advocated by the experimental

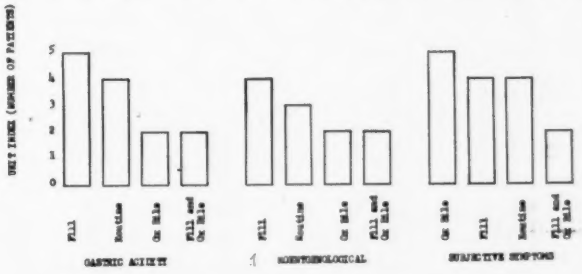

Fig. 2—Response of patients with simple duodenal ulcer to varied forms of therapy.

work of Casimir Funk and his associates[14]. The author was inclined to test the efficacy of these inexpensive drugs in view of recent favorable clinical reports[15,16].

Method of Study

Twenty patients in private practice were studied. This procedure was thought best since personal observation, supervision, and treatment were handled by one person. With more individualized attention there would be no doubt of the patients' cooperation. After a detailed history, physical examination, gastrointestinal x-rays, and gastric analysis a diagnosis of duodenal ulcer was made. No questionable nor indefinite diagnosis was included in the study.

The patients were separated into the following groups: (1) *Routine*—patients received the available antiulcer medications such as banthine, prantal, sebella, gelusil, amphojel, kolantyl, or an especially prepared alkaline capsule; (2) *F111 group;* (3) *Ox-bile group;* (4) *Combination of F111 and ox-bile.* It seemed best that the present antiulcer drugs should be compared to those usually prescribed for such a condition. The special drugs under investigation were given one, two, or three tablets after each meal; one tablet before retiring; and one tablet

if the patient were awakened during sleep. The amount varied depending upon the severity or recurrence of complaints. Patients have been observed from six to twelve months depending upon favorable or unfavorable response. Patients were interviewed and examined monthly. Roentgenological surveys to denote any change were made at three month intervals. Diets were bland in character, becoming more liberal with the patient's clinical improvement[4].

TABLE I

SYMPTOMATOLOGY AND LABORATORY DATA OF SIMPLE DUODENAL ULCER PATIENTS BEFORE AND AFTER VARIED MEDICAL THERAPY. EXPRESSED IN NUMBER OF PATIENTS AND PERCENTAGES

Symptoms	Routine		F111		Ox Bile		F111 & Ox Bile		Total of Combined Therapies			
	Before	After	Before	After	Before	After	Before	After	Before		After	
									No.	%	No.	%
Belching	5	4	3	1	2	1	2	0	12	60	6	30
Bleeding	1	0	1	1	2	0	1	0	4	20	1	5
Constipation	3	2	3	1	0	1	1	1	8	40	5	25
Diarrhea	1	0	0	0	2	2	1	1	4	20	3	15
Epigastric Distress	5	4	2	1	2	3	3	2	13	65	11	55
Heartburn	4	2	2	1	3	3	3	1	12	60	7	35
Hunger Feeling	2	1	2	2	3	0	4	3	10	50	6	30
Pain	1	1	2	0	2	2	5	3	10	50	5	25
Vomiting	1	1	1	0	0	0	3	1	5	25	2	10
Sourness	4	2	3	0	2	0	3	2	12	60	4	20
Nausea	1	0	2	0	0	0	1	1	4	20	2	10
Weight												
steady	5	3	2	2	1	1	2	3	10	50	9	45
gain	1	2	1	2	3	4	1	0	6	30	8	40
loss	0	1	1	0	1	0	2	2	4	25	3	15
Improvement												
clinical		4(80%)		4(80%)		5(100%)		2(40%)			15	75
x-ray		3(60%)		4(80%)		2(40%)		2(40%)			11	55
gastric		4(80%)		5(100%)		2(40%)		2(40%)			13	65
Psychoneurosis	1	0	1	1	4	1	3	1	9	45		

CLINICAL COURSE

Twenty patients with definite diagnosis of duodenal ulcers were studied. Six females and fourteen males ranging in ages from 30 to 59 were included. The most common complaints were belching, heartburn, sourness in the mouth, or epigastric distress or "lump" after meals. Pain and hunger feeling were present in 50 per cent of the patients. There are so many indefinite and atypical complaints in peptic ulcer patients that one cannot be so dogmatic as to

insist on a characteristic, diagnostic history[16]. Nine out of twenty patients (45 per cent) had a marked emotional, unstable, nervous system influencing the

TABLE II

EFFECT ON GASTRIC ACIDITY BEFORE AND AFTER VARIED TYPES OF MEDICAL TREATMENT FOR DUODENAL ULCER PATIENTS EXPRESSED IN CLINICAL UNITS

		Routine Antiulcer Therapy							
		Treatment							
		Before				After			
Case No.	Patient	Free	Total	Combined	Organic	Free	Total	Combined	Organic
1	S. G.	36	53	10	7	32	40	2	6
2	S. G.	38	52	7	7	22	44	12	10
3	R. S.	40	58	11	7	28	32	0	4
4	E. S.	18	36	9	9	22	40	10	8
5	M. G.	40	69	19	10	20	42	15	7
	Arith. Mean	34	53	11	8	24	39	8	7
	Organic Potassium Salts (F111)								
6	B. B.	42	60	10	8	28	38	5	5
7	G. L.	30	48	12	6	25	33	5	3
8	L. P.	55	84	11	18	41	60	8	11
9	W. McL.	51	70	13	6	40	58	12	6
10	S. W.	65	126	52	9	28	44	0	16
	Arith. Mean	49	77	19	9	32	46	6	8
	Ox-bile Powder								
11	M. H.	38	52	7	7	40	50	5	5
12	H. R.	70	92	7	15	68	88	4	16
13	M. S.	23	55	20	12	28	48	14	6
14	I. R.	35	80	25	20	30	52	12	10
15	A. C.	50	64	4	10	38	50	6	6
	Arith. Mean	43	68	12	13	40	57	8	9
	Organic Potassium Salts (F111) + Ox-bile Powder								
16	F. D.	34	49	10	5	30	50	10	10
17	M. O.	53	89	12	24	55	80	10	15
18	F. R.	32	78	21	25	27	51	14	10
19	A. R.	60	88	15	13	25	40	9	6
20	A. W.	60	72	4	8	50	73	13	10
	Arith. Mean	47	74	12	15	37	59	12	10

patient clinically. The overall picture showed an effect on belching, heartburn, pain, and sourness in 50 per cent and more of the patients. Diarrhea, epigastric

distress, and hunger feeling were not entirely relieved. Weight was steady or increased in sixteen patients (80 per cent) (Table I).

Gastric Acidity

Free and total acidity were reduced in all forms of therapy. The effect on combined and organic acids had no bearing upon the present study (Table II). The reduction before and after therapy of the varied groups showed the greatest percentage reduction with F111; routine therapy; F111 and ox-bile; ox-bile, in the order enumerated (Fig. 1). The reduction of free and total acidity after therapy was as follows: F111—34 and 40 per cent; Routine—29 and 26 per cent; F111 and ox-bile—21 and 20 per cent; ox-bile—7 and 16 per cent (Table

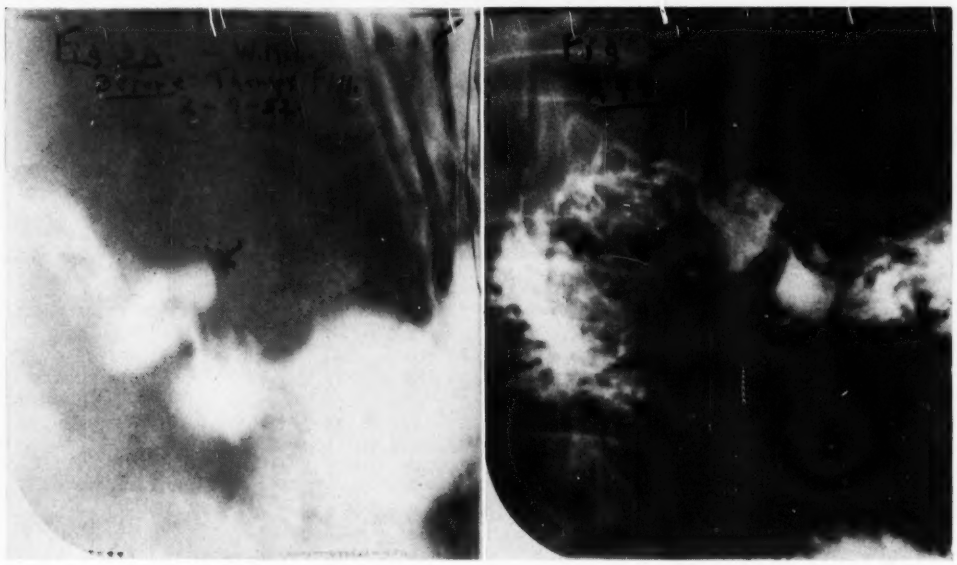

Fig. 3a Fig. 3b

Fig. 3a—Before F111 therapy (W. McL.): Duodenal cap deformed with niche on lesser curvature, pseudodiverticulum on greater curvature; eccentric pyloric canal.

Fig. 3b—Thirteen months after F111 therapy (W. McL.): Practically normal duodenal cap. Prolapse gastric duodeni noted. Improvement.

III). If each patient with a positive response is considered as a unit, we find the following: F111—5 units; routine—4 units; ox-bile—2 units; F111 and ox-bile —2 units (Fig. 2).

Roentgenological Studies

Although the history may have been suggestive of a peptic ulcer, no patient was considered for treatment unless there was direct roentgenological evidence of the same; namely, a deformed duodenal cap with or without a niche; indentation of the greater curvature opposite the niche, a pseudo-

diverticulum, phthisis bulbi (nonfilling) and an eccentric pyloric canal[18]. Such strict criteria were necessary in order to see the effect and improvement under the respective medication and to preclude any questionable roentgenological change to a normal structure. The greatest changes roentgenologically were: F111—80 per cent; routine—60 per cent; ox-bile—40 per cent; and F111 and ox-bile—40 per cent (Table I). Expressed as units were F111—4; routine —3; ox-bile—2; and F111 and ox-bile—2 (Fig 2).

TABLE III

COMPARATIVE EFFECT OF VARIED MEDICAL THERAPIES UPON DECREASE OF GASTRIC ACIDITY IN SIMPLE DUODENAL ULCER PATIENTS, EXPRESSED IN CLINICAL UNITS AND PERCENTAGES

Arithmetical Mean Gastric Acidity Values

Method of Therapy	Free	Total	Combined	Organic
Routine antiulcer				
Before	34	53	11	8
After	24	39	8	7
Decrease in Units	10	14	3	1
Decrease—Percentage	29	26		
Potassium Acid Acetate (F111)				
Before	49	77	19	9
After	32	46	6	8
Decrease in Units	17	31	13	1
Decrease—Percentage	34	40		
F111 and Ox-bile				
Before	47	74	12	15
After	37	59	12	10
Decrease in Units	10	15	0	5
Decrease—Percentage	21	20		
Ox-bile Powder				
Before	43	68	12	13
After	40	57	8	9
Decrease in Units	3	11	4	4
Decrease—Percentage	7	16		

It is evident that the deformed duodenal caps did not become normal in many cases (Table I). If there were a lessening of the deformity (Figs. 3a, b), an absence of the previous duodenal niche (Figs. 4a, b), or a practically normal appearing duodenal cap (Figs. 5a, b) these were considered as improvement. Recurrence of severe epigastric pain, whether due to another episode of peptic ulcer (patient M. O., Fig. 6c) or marked emotional upsets (patient M. S., Fig. 7b) may be noted in individuals with marked psychoneurosis. This has a marked

detrimental effect on the therapy and roentgenological improvement (M. O. and M. S.).

Subjective Symptoms

Progress was noted in patients by the history and the examination after the respective therapy. This may have been considered in spite of some complaints present during the period of observation. Indeed all subjective complaints did not disappear. One must be guided by the general appearance of the patient, his state of well being, the diminution, recurrence, and severity of both subjective and objective findings.

As mentioned above, belching, heartburn, epigastric pain and a "sour taste" in the mouth were relieved in 50 per cent of the patients (Table I). Diarrhea, epigastric distress or "lump" after meals and hunger feeling helped by food or

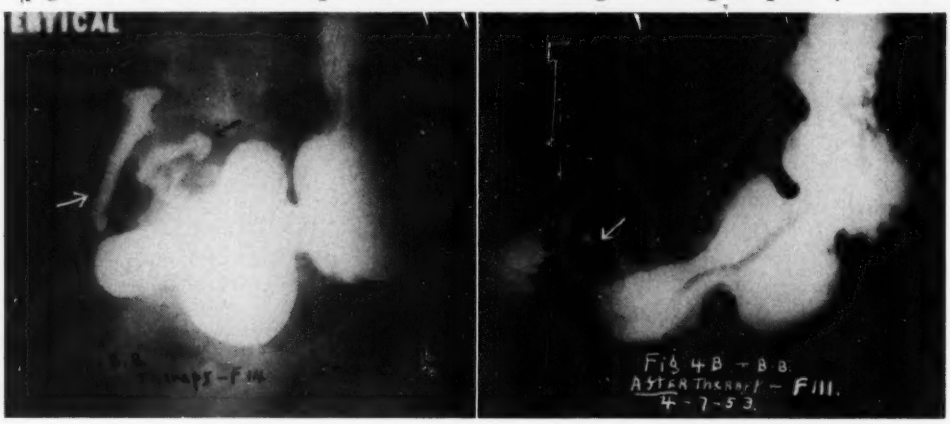

Fig. 4a Fig. 4b

Fig. 4a—Before F111 therapy (B. B.): Duodenal cap deformed with niche on lesser curvature. Superior border elongated with pseudodiverticulum. Pyloric gap.
Fig. 4b—Eleven months after F111 therapy (B. B.): Pyloric gap. Cap indistinctly filled. Improvement.

medications were not entirely relieved. Constipation and diarrhea varied depending upon the nervous status of the individual and whether there have been any emotional factors present. This was especially true in those patients in whom psychoneurosis played an important role. By chance this condition was the most frequently encountered in the group of patients under the ox-bile therapy (Table I).

Regardless of what form of medication the patient may take, the drug must be increased, given more frequently, and personal encouragement by the physician are essential. Patients M. O. and M. S. experienced more subjective complaints during emotional upsets in spite of being also treated by a psychoanalyst. Indeed, a recurrence of gastrointestinal hemorrhage occurred during the combined medical and psychoanalytical treatments in the above two patients.

It is of interest that there was clinical improvement in all the patients under ox-bile therapy (100 per cent); while only 40 per cent improved by x-rays and gastric analysis criteria (Table I). F111 and the routine regimen showed 80 per cent improvement while ox-bile and F111 combination only 40 per cent. If expressed by units there was clinical improvement with ox-bile—5 units; F111 and routine—4 units; while the combination of F111 and ox-bile only 2 units (Fig. 2).

Potassium and Electrocardiographic Studies

Normal serum potassium and electrocardiograms were obtained in five patients with acute peptic ulcer syndrome. This number of patients is not sufficient to draw any final conclusions as to whether there may be some

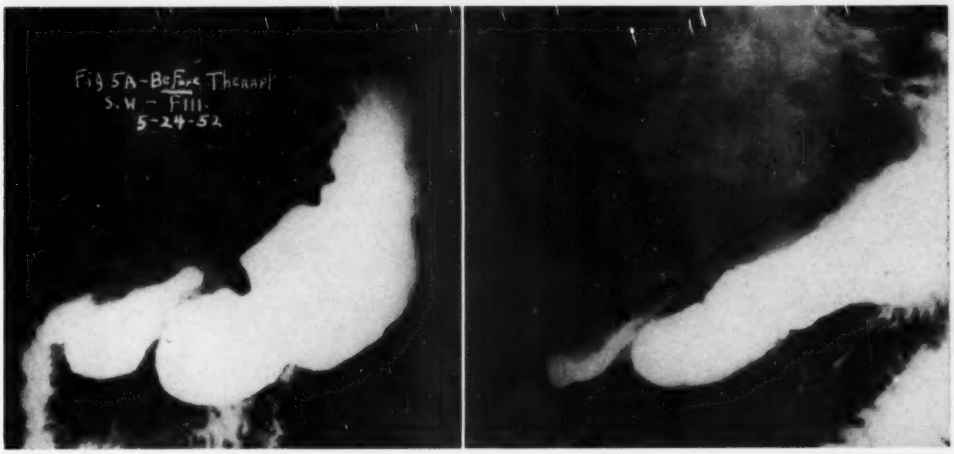

Fig. 5a Fig. 5b

Fig. 5a—Before F111 therapy (S. W.): Eccentric pyloric canal. Duodenal cap elongated with pseudodiverticulum.

Fig. 5b—Six months after F111 therapy (S. W.): Duodenal cap much smaller and irritated. Pseudodiverticulum absent. Improvement.

disturbance in the potassium ion mechanism in such patients. A larger series is essential. Many of the electrocardiograms in other simple peptic ulcer patients, however, do not show any potassium ion disturbance. This may occur in patients with complicated duodenal ulcers producing marked retention, vomiting or diarrhea.

Case Reports

W. McL. (*patient* #9), male, age 40, gives a 10 year history of gastrointestinal disturbance affected by "seasonal changes". For the past month, persistent epigastric pain radiating to the back and not relieved by food or alkalis as well as hunger pains were experienced. Hematemesis on 2 occasions was noted. Physical examination revealed the patient to be very nervous, anxious and

restless. Abdominal palpation produced marked epigastric tenderness. On percussion tenderness was elicited posteriorly in the spinal region. X-rays showed (Fig. 3a) eccentric pyloric canal; a niche on the lesser curvature and pseudodiverticulum on the greater curvature of the duodenum. There was marked pylorospasm. The patient received medications such as codeine sulfate, phenobarbital, prantal and gelusil. Since the results were inconsistent, the patient was placed on the organic potassium salts (F111), ten tablets per day. Improvement, especially hunger pains was noted. Months after being on this therapy the patient passed tarry stools without any ill effects. In spite of this bleeding episode the x-rays showed a practically normal duodenal cap with a prolapse of the gastric mucosa into the duodenum (Fig. 3b).

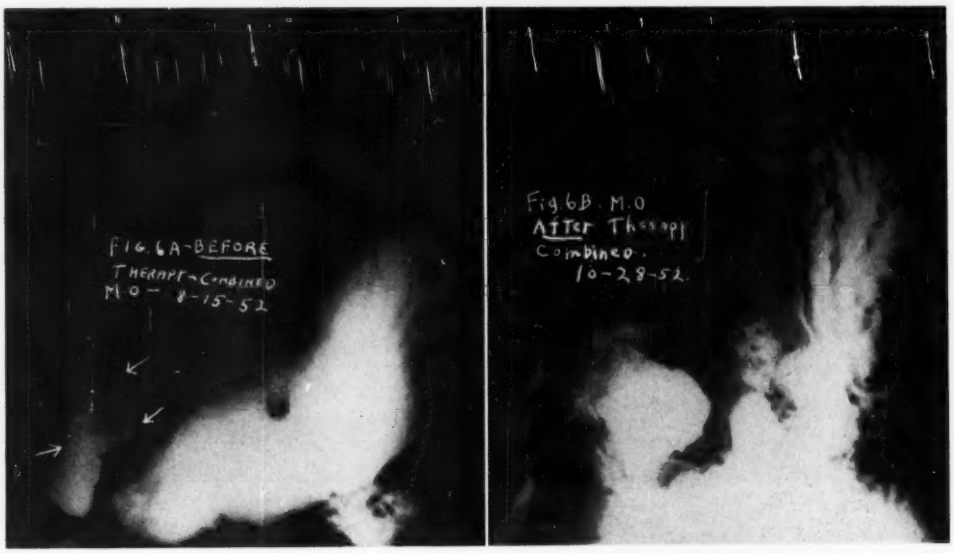

Fig. 6a Fig. 6b

Fig. 6a—Before combined therapy (M. O.): Eccentric pyloric canal. Duodenal cap deformed with niche on lesser curvature and pseudodiverticulum on greater curvature.

Fig. 6b—Two months after combined therapy (M. O.): Duodenal cap appears normal with absent previous roentgenological signs.

B. B. (patient #6), female, age 30, had experienced gastrointestinal complaints with heartburn relieved by alkalis, abdominal pains after meals, and backache of seven years' duration. There had been a weight loss of 40 pounds. Nervous instability was very pronounced. Examination revealed a thin asthenic, restless type of individual. Epigastric tenderness was very pronounced. Gastric lavage produced a large fasting residue with retention of food. The x-rays showed a pronounced 4 hour residue which was not present after frequent gastric lavages and conservative medical therapy. The duodenal cap was markedly deformed with a niche on the lesser curvature and pseudodiverticulum-like projection on the greater curvature (Fig. 4a). There was recurrence of abdominal pains,

nausea and vomiting whenever factors prevailed to disturb a highly unstable nervous system. In spite of these emotional bouts the patient became more stabilized, gained weight and tolerated food with little difficulty. The patient had especially prepared antiulcer capsules, pavatrine with phenobarbital, and papaverine. Since banthine produced a markedly dilated colon simulating a megacolon, it was discontinued. Kolantyl and prantal were of no aid. The patient was then placed on the organic potassium salts (F111), 9 to 12 tablets daily. Under this therapy the x-rays showed the pyloric gap to be present. The duodenal cap was indistinctly filled. The pseudodiverticulum and niche of the duodenal cap were absent (Fig. 4b), and the subjective symptoms diminished.

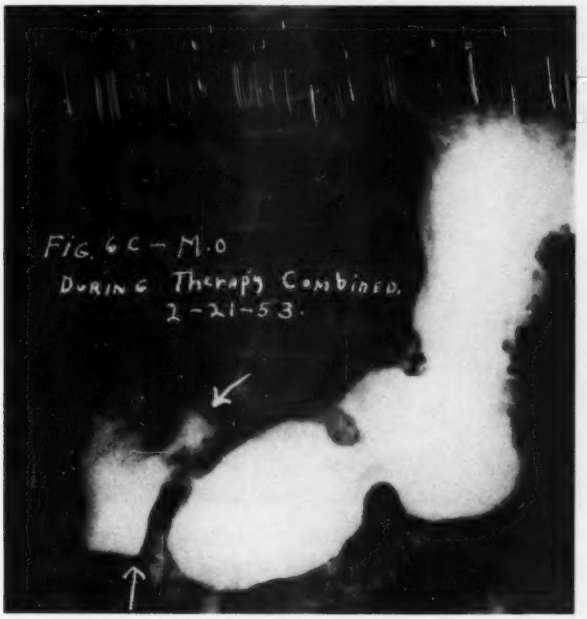

Fig. 6c—Six months after combined therapy (M. O.): Recurrence of direct x-ray signs during medical and psychoanalytical therapies. No improvement.

S. W. (*patient #10*), male, age 58, had two years' history of weight loss, heartburn, belching and epigastric "pressure" on retiring. The appetite was good. Constipation was very marked. The physical examination especially the abdomen was of no significance. The x-rays showed a distorted and elongated duodenal cap, a pseudodiverticulum of the greater curvature of the cap and an eccentric pyloric canal (Fig. 5a). Symptoms varied with no pronounced improvement under varied antiulcer drugs such as sebella, kolantyl, and alkalis. Since sourness in the mouth with constipation persisted under ox-bile powder therapy, the patient was placed on F111 therapy, taking 6 to 8 tablets daily. Constipation was the only complaint noted. X-rays revealed a smaller duodenal cap, with evidence of irritation. The pseudodiverticulum of the cap was not present (Fig. 5b).

M. O. (*patient #17*), female, age 30, had been diagnosed as having a duodenal ulcer for three years, during which times there had been recurrent gastrointestinal complaints. The patient had two attacks of bleeding and a marked anemia when first examined by the author. Severe psychoneurosis and marked emotional instability were prevalent. The patient had been placed on antiulcer therapy especially banthine, sedatives and narcotics to overcome the severe abdominal pains. X-rays showed an eccentric pyloric canal; a niche on the lesser curvature and a pseudodiverticulum on the greater curvature of the duodenum (Fig. 6a). Under combined therapy of organic potassium salts (F111) and ox-bile powder there was an improvement both subjectively and roentgenologically. The latter showed the duodenal cap to assume a practically normal appearance. The previous direct x-ray signs of niche and pseudodiverticulum were absent (Fig. 6b). Because of a pronounced fear for a recurrent

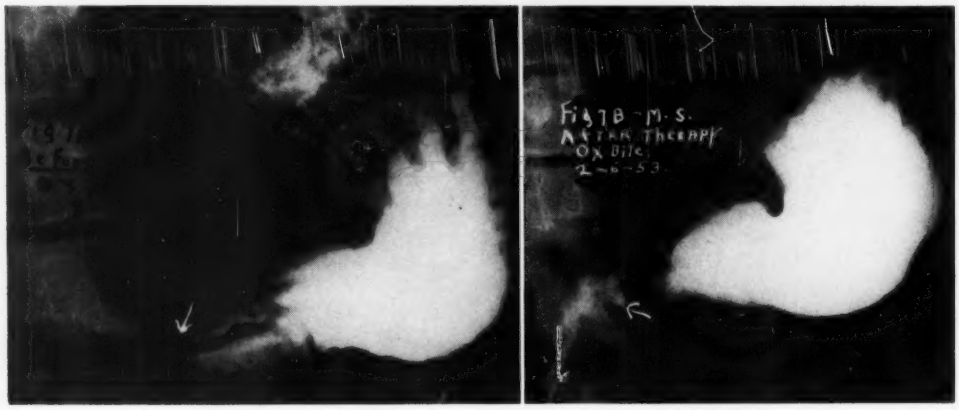

Fig. 7a Fig. 7b

Fig. 7a—Before ox-bile powder therapy (M. S.): Phthisis (nonfilling) duodenal cap. After hemorrhage.

Fig. 7b—Six months after ox-bile powder therapy (M. S.): Duodenal cap more deformed during medical and psychoanalytical therapies. No improvement.

hemorrhage, disturbed domestic factors and extreme nervousness the patient was also under the care of a psychoanalyst. No marked improvement was noted. Hunger pains relieved by food and nocturnal pains were prevalent. The x-rays showed a recurrence of a deformed duodenal cap as present before therapy (Fig. 6c). It was felt that both the medical and psychoanalytical treatments were of no avail. Surgery was performed at the request of the patient.

M. S. (*patient #13*), male, age 33, was known to have a duodenal ulcer for the past 12 years. The patient was hospitalized for attacks of bleeding in 1941, February 1949, March 1949. The first episode of bleeding occurred at the age of 12. The severity and recurrence of complaints depended upon the emotional upsets produced both by business and domestic difficulties. Epigastric distress, hunger pains with radiation to the back, belching, and sourness in the mouth

were present at varied intervals. Symptoms abated when domestic calmness and improved business conditions prevailed. Psychoanalysis had some effect in producing self-reliance and a lessening of an inferiority complex. X-rays showed phthisis bulbi (after the third attack of hemorrhage); pylorospasm; pseudodiverticulum of the cap; and a pyloric gap (Fig. 7a). The patient had especially prepared alkaline powders, gelusil, resinat, mucotin and pavatrine with phenobarbital. Diarrhea with abdominal pains, hunger pains, and belching were pronounced during business recession. The patient was placed on ox-bile powder therapy with some clinical but not roentgenological improvement. The x-rays showed the duodenal cap to be more deformed (Fig. 7b). It was felt that the medical antiulcer therapy did not improve the patient's condition. The more stabilized nervous system may have been produced by psychoanalytical therapy.

Summary and Conclusions

1. There is no definite etiological factor for the cause of peptic ulcer.

2. At present there is no specific medical therapy for peptic ulcer based on pathogenesis.

3. Drugs for peptic ulcer give varied results depending upon the enthusiasm of the observer.

4. Recent anticholinergic drugs have not proven to be the specific par-excellence form of treatment.

5. A new approach to antiulcer medication based upon local chemical changes has been tried.

6. Based upon the work of Casimir Funk and his associates organic potassium salts (F111) and bile powder products (ox-bile) have been tried in a small group of noncomplicated peptic ulcer patients.

7. Organic potassium salts (F111) decreased the volume and acidity of gastric juice from Shay rats and the patients herein reported.

8. It was the first time that an antiulcer drug was utilized in an acid medium of pH 4.5 rather than alkaline as with most antiulcer medications.

9. Organic potassium salts (F111) showed better response to roentgenological improvement and diminution of gastric acidity than the present available antiulcer drugs.

10. Many extragastric factors affect ideal results in the treatment of peptic ulcer patients such as cooperation, emotional instability and exact dosage.

11. Since the new medications mentioned herein compare favorably to the present available antiulcer drugs and because of its relatively low cost to the patient, it seems worthwhile that further clinical investigation should be pursued.

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THE RUPTURE OF THE ECHINOCOCCUS CYST OF THE LIVER INTO THE BILE DUCTS*†

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I was prompted to choose this subject for two reasons. First, the considerable experience of Greek surgeons in the diagnosis and treatment of echinococcus diseases and second the rare occurrence of this disease in the United States of America.

Since the subject is extremely extensive and much has been written about it I shall confine myself to the essential points. Before I enter upon the specific discussion of the subject, however, I feel that it would be of interest to briefly remark about the disease in general. The echinococcus cyst or hydatid disease

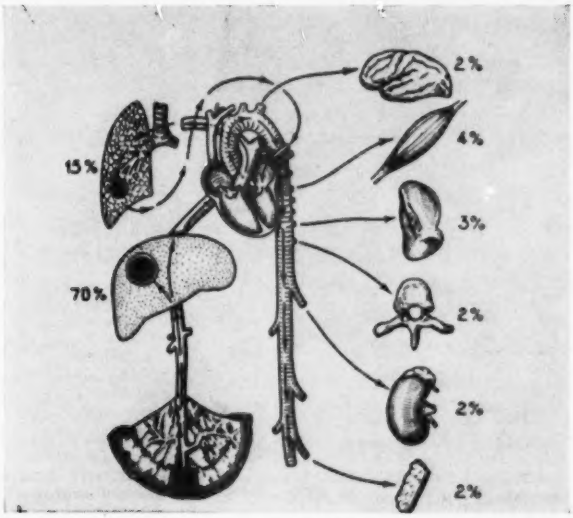

Fig. 1—Percentage incidence of localizations of echinococci in various organs: 85 per cent by venous blood (left); 15 per cent by arterial blood (right). (After Ivanissevich)

is caused in the human body by the larval stage of the tapeworm, *Taenia echinococcus*. The egg of the *Taenia echinococcus* finds its way into the system via infected vegetables or water. Infection may also take place directly through dogs who may be permanent hosts of the parasite and whose feces may contain vast numbers of echniococcus eggs. Ivanissevich depicted (Fig. 1) the localization and percentage of echinococci in various organs. It will be noted that the liver

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is the most commonly affected organ accounting for 70 per cent of all cases. More detailed accounts are obtainable from the bibliography, particularly the treatises of Dévé[6], Hosemann, et al[16], and Dew[10].

Greece is among the countries where echinococcus disease is most widespread. According to the statistics of Toole[27,28,29] and Makkas[20], 11,107 cases of echinococcus cysts were operated upon in hospitals and clinics of Greece, within a period of fifty years. Of these, 67 per cent were liver cases.

The diagnosis of echinococcus cyst of the liver as well as other organs does not present great difficulties in countries where the disease is common. In cases without complications the operation is a comparatively easy one with an average

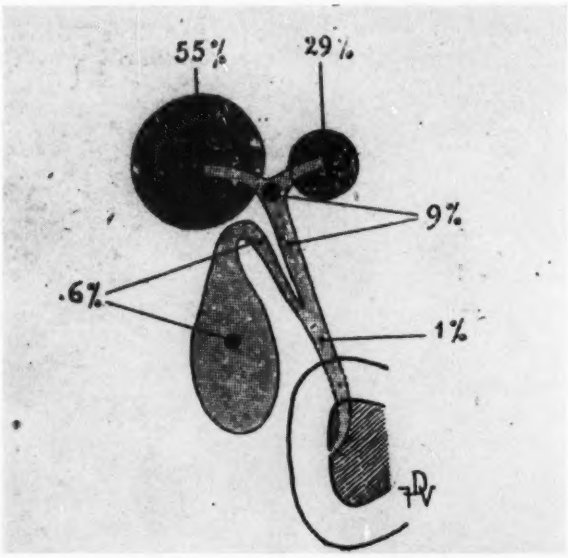

Fig. 2—Sites and percentage incidence of ruptures in the biliary system according to Dévé.

mortality of 4.8 per cent[20]. In complicated cases, however, where there is either necrosis of suppuration of the cyst or rupture into the peritoneum, the bile ducts, or pleura and bronchi, the diagnosis and treatment are likely to produce considerable difficulties and an increase in mortality. Particularly with ruptures into the bile ducts the mortality is estimated according to statistics to be as high as 30-40 per cent[8,18].

History

The first to study the subject were Davaine (1860), Trousseau (1865) and Frerichs (1868). In 1883, Berthaut in the course of a special study examined thirteen cases of echinococcus cysts of the liver which had ruptured into the bile ducts; twelve being confirmed by autopsy.

The interest of the surgeons was aroused after the publication of Quenu's and Duval's[24] presentation before the Society of Surgery of Paris in 1906 and Lecène's and Mondor's[19] treatises in 1914. From 1916 onward, Argentine surgeons such as Abadie, Hernandez and Finochietto[12], took up the study of the subject. Finally from 1919 until 1925, Dévé, who was responsible for a great number of treatises on echinococcus cysts undertook systematic research. The latter author also collected all the cases recorded up to this time from the bibliography, amounting to 267. Since then all studies of the subject have been based upon the observations recorded by Dévé and his co-workers.

In Greece the study of the rupture of echinococcus cysts of the liver into the bile ducts was reported in 1905 in the publication of a case history by Makrykostas[21]. In 1927, Sotropas[25], published three additional case histories. In 1931, Karajiannopoulos and Tofaridis[17], reported six cases and Geroulanos[14], one. In 1932, Kourias[18], published a detailed study based on fifteen cases and finally in 1936, Christeas[5], reported another five cases. If we add to this the ten cases mentioned in Toole's statistics[27], and the four cases to be subsequently discussed in this paper it would make a total of 45 cases. The total number of cases reported up to 1936 in the International Bibliography was approximately 315 according to Christeas[5].

Case Histories

Case 1:—Male patient, aged 52, complained at intervals varying from 6 to 8 months from 1934 of biliary colic accompanied by fever, jaundice and altered coloration of the stools. In January, 1943, the patient was operated upon for echinococcus cysts of the liver which had ruptured into the bronchi. After operation (transpleural laparotomy) a fistula remained discharging bile and membranes. There was also considerable expectoration of bilious sputum. On September 27, 1947, the patient was admitted to the Second Surgical Clinic, University of Athens where two operations were carried out for the purpose of detecting the site of the rupture of the echinococcus cyst of the liver into the bronchi. The result, however, was not quite satisfactory. Two months later the patient again showed a rise in temperature with intense pain in the right upper hypochondrium and a considerable enlargement of the liver. The patient was subjected to an exploratory laparotomy with the aim of finding the echinococcus cyst and locating the common bile duct. The latter was eventually found in a state of dilatation. After the common bile duct was opened there resulted a copious flow of membranous fragments. When these obstructions were finally removed a free flow of bile ensued. By probing with the finger we established that the passage was unobstructed. We desisted from probing any further for the echinococcus cyst as the general condition of the patient prevented our doing so. After drainage of the common bile duct had been established we sutured the incision. The patient died on the same day with symptoms of severe cholangitis. It seems that in this case a rupture into the bile ducts preceded the rupture into the bronchi; the latter being a complication of the former.

Case 2:—Male patient, aged 36, suffered with right upper quadrant colic since 1949, accompanied by vomiting and jaundice for periods lasting from three to four days. A fortnight before admission to the hospital, the same symptoms were accompanied by fever (101 degrees) and chills. The patient was admitted to the Second Surgical Clinic, University of Athens on November 11, 1949, with the diagnosis of suppurated echinococcus cysts of the liver, with a possible rupture into the bile ducts. Clinical examination revealed a mild jaundice, an enlarged liver and tenderness on pressure in the right hypochondrium. X-ray examination revealed no displacement of the diaphragm. The leucocyte count was 9,000 per cm. with 7 per cent eosinophiles. The stools were normal. After preliminary preoperative care, operation was performed. Adhesions between omentum and liver were found. The liver was enlarged and two echinococcus cysts were found, one on the anterior and the other on the inferior surface. Both were dead and contained multitudes of bile-stained, collapsed daughter cysts. The common bile duct was dissected and upon opening it, it was noted to be unobstructed and there resulted a free flow of clear bile. The duct as well as the cyst were drained. The postoperative course was uneventful and the patient was discharged two months later. In this case a rupture was not confirmed by operation; its existence however was considered likely by the symptoms.

Case 3:—Male patient, aged 32 years who complained for seven months of periodically recurring pains in the right hypochondium accompanied by bilious vomiting. His family physician diagnosed the condition to be cholelithiasis and prescribed conservative medical treatment. Twenty days before his admission, the patient became jaundiced and the stools altered in color, unaccompanied by fever. The patient was admitted to the Second Surgical Clinic, University of Athens, on April 4, 1950. Clinical examination disclosed obvious jaundice, an enlarged liver and rounded margin. X-ray examination revealed restricted mobility of the right diaphragm. Leucocyte count was 10,000 per cm. with 39 per cent eosinophiles. The Casoni intradermal test was positive, three plus. The stools were acholic but no membranous substances were found. The preoperative diagnosis was echinococcus cysts of the liver with rupture into the bile ducts.

At operation an enormous unilocular cyst was found on the inferior surface of the liver containing about two kilograms of bile stained fluid. The mother cyst was dead and collapsed. Owing to the solid adhesions to the surrounding organs and the poor general condition of the patient we did not search for the common bile duct but confined ourselves to marsupialisation and drainage of the cavity.

The postoperative course was excellent. The patient was discharged on the 15th postoperative day. Since then he has been in good health. A rupture into the bile ducts was not confirmed by operation. Its likelihood, however, was strengthened by the symptoms and the course of the disease.

Case 4:—Female, aged 50 years, was operated upon on June 1, 1949, with the operative finding of an echinococcus cyst of the liver containing dead

daughter cysts. Drainage was established and the patient discharged from the hospital one month after operation. Two years later, the patient was readmitted to the Second Surgical Clinic, University of Athens, complaining of intense pains in the right hypochondrium accompanied by fever and chills. Physical examination revealed considerable enlargement of the liver which was tender to pressure. An elastic mass could be palpated in the right lumbar region which was directly connected with the enlarged liver. There was mild jaundice. The stools were normal and no membranes were discovered. The leucocyte count was 9,000 per cm. with 6 per cent eosinophiles. The admission diagnosis was a new suppurated echinococcus cyst of the liver or suppuration of remains of the old cyst. At operation, a cyst was found projecting from the inferior surface of the liver, and it was full of debris of membranes and bile-stained fetid pus. At the upper posterior wall of the cavity an orifice was found through which the index finger could be inserted into another cavity from which flowed a certain amount of bile. This cavity may have been the gallbladder. Upon withdrawal of the index finger a pea-sized gallstone with rounded edges was evacuated. It was exactly like the stones found in the gallbladder. The solid adhesions and the infectious contents of the cyst did not permit a detailed examination. We therefore limited ourselves to evacuating the contents of the cyst, marsupialisation and drainage of both the echinococcus cyst and the supposed gallbladder. In this instance the operative findings permit the assumption of a rupture of the echinococcus cyst into the gallbladder.

During the first postoperative days there was an abundant flow of bile containing membranous debris. Forty days after operation the bile stopped flowing, the drain was removed and soon afterwards the wound healed. The patient left the hospital in continued health.

Discussion

In three of the four cases a rupture into the biliary ducts was either preoperatively diagnosed or its possibility considered. A rupture into the bile ducts was definitely established at operation in two cases, (first and fourth). The common bile duct was drained in two cases, (first and second) and in one case we were under the impression of having drained the gallbladder. The echinococcus cyst was drained in all cases except the first in which we refrained from searching for the cyst. There was a fatal case i.e., the one in which there had been a rupture into the bronchi. Modern pre- and postoperative care was employed in the operated cases.

Statistically rupture of echinococcus cysts into the biliary ducts occurs with similar frequency in both sexes. Dévé[6], in a series of 240 cases tabulated 121 ruptures in males and 119 in females. He estimated that in a hundred cases of echinococcus cysts of the liver about five to ten per cent rupture into the bile ducts. Kourias[18], estimated the incidence as 3.75 per cent and Sotropas[28], as

4 per cent. We experienced four cases of such rupture in a total of eighty-two cases of echinococcus cysts of the liver. The most frequent occurrence was in persons aged from thirty to fifty.

Formerly it was believed, that this complication occurred more often in cysts located on the inferior surface of the liver chiefly in the vicinity of the hilum. Dévé recorded that cysts located on the superior and exterior surface of the liver were more likely to rupture. There is some difference of opinion as to the direction of rupture so that the figures vary considerably. Thus Lecène and Mondor[19], found that out of a total of one hundred instances, twenty-four had ruptured into the common bile duct, thirty-three into the gallbladder and cystic duct and forty-three into the hepatic ducts. Dévé, on the contrary depicted (Fig. 2) the following figures: 84 per cent of all ruptures occurred into the intrahepatic bile ducts, particularly into the right lobe, 9 per cent into the hepatic duct, 6 per cent into the gallbladder and only 1 per cent into the common bile duct. Dew[10], in his monograph, estimated the frequency of ruptures into the intrahepatic bile ducts at 55 to 60 per cent.

Judging from our limited personal experience we are of the opinion that the site of the rupture is not always easy to locate during the operation. The size of the ruptured cysts ranges from that of a mandarin to that of a child's head or even larger. Undoubtedly there is some relation between the size of the cysts and their frequency of rupture. A large number of ruptured cysts contain daughter cysts, with a reported incidence of about 93 per cent by Dévé, and Duprey[11], in his series of 55 ruptures.

Suppuration may occur in these cysts with as high as a 55 per cent incidence. In 10 per cent of these, gas formation may occur as the result of infection by anaerobic organisms[6,18].

Pathogenesis

Many theories have been proposed regarding the causes and mechanism of ruptures. Thus Quénu and Cauchoix[25] suggest that ruptures are due to mechanical pressure from an existing gallstone. Berthaut and Carle[4], maintain that an intermediate abscess between the adventitia which encloses the echinococcus cyst and the wall of a bile duct commonly precedes a rupture. Finally, Dévé[6], again insists that the rupture follows a local necrosis of the wall of a bile duct in consequence of the pressure caused by the growing echinococcus cyst. We are of the opinion that all three factors may be considered as contributing to a rupture since they are responsible for a gradual thinning and corrosion of the wall of the bile duct.

The periodical recurrence of the symptoms of obstruction of the bile duct may be attributed to the existence of daughter cysts or the necrosis of the mother cyst. Automatic clearing of the obstructed passage occurs fairly often and more readily than in the case of an obstruction due to a gallstone. This is chiefly

due to the soft and gelatinous nature of the obstructing matter which permits it to mold itself and slip through the common bile duct and the ampulla of Vater, provided the amount of membranous matter which fills the passage is not excessive. Additional contributory factors to be considered are: the increase of pressure within the bile ducts proximal to the obstruction, the movements of the diaphragm as well as the occasional increase of intraabdominal pressure.

Symptomatology

In typical cases three main symptoms are prominent: pain, jaundice and passage of membranes in stools (hydatidenteria) or vomitus (hydatidemesia). Moreover, secondary symptoms may exist, such as fever, enlargements of the liver and anaphylactic manifestations.

The pain is as a rule, acute, intense and localized in the epigastrium or in the right hypochondrium with radiation to the corresponding shoulder or the right lumbar region. It may occur after meals, after catharsis[6] or after more or less severe trauma to the abdominal wall[10]. The pain is often so intense as to cause the patient to double up as in a case of liver colic. It is usually accompanied by anaphylactic symptoms (hydatid anaphylaxis) such as dyspnea, collapse, nausea, vomiting, collapsed pulse and cutaneous manifestations (hydatid rash) sometimes followed by pyrexia[10]. These symptoms are due to the absorption of echinococcus fluid (antigen) by the sensitized organism[10]. The duration of pain varies from minutes to hours and may then suddenly disappear. In 10 per cent of the cases the pain and other manifestations are not so pronounced. Usually the pain recurs. Upon inquiry a history of repeated attacks is often obtained. In two of our cases there had been over five attacks within a period of six months.

Jaundice was absent in only 7 per cent of all ruptured cases. Its intensity varies according to the degree and duration of obstruction. Sometimes it manifests itself rather late. Usually it is obvious and accompanied by altered color of the stools and pruritus. In 80 per cent of the cases there was a relapse. Sometimes its persistence is due not to the original obstruction but to an additional complication of cholangitis or hepatitis. Frequently, the membranes in the stools escape detection because the doctor or the patient do not look for them, or because of their small size. At other times there is an abundant discharge of membranes or daughters within watery and bilious stools which hardly escape notice. Dévé appropriately called this, *"Debacle hydatique cholodechovaterienne"*. The detection of the membranes in the vomitus is less difficult. Of the secondary symptoms, mention may be made of the enlargement of the liver[6] and the occasionally confirmed dilatation of the gallbladder. Finally fever is a regular symptom being absent in only 15 per cent of the cases[6]. It is usually intermittent with sweating and rigor and is due to the suppuration of the cyst and the coexisting cholangitis.

Course and Prognosis

As can be gathered from statistics[6,18] the course of this complication can be grave, and in cases not operated upon, the mortality is extremely high. Cases are on record, however, which have undergone a spontaneous cure once all the membranous remnants, after rupture had been eliminated. Duprey[11], in an exhaustive review estimates that instances of spontaneous cure constitute 23 per cent. Such cases have also been recorded in Greece by Makkas and Karajiannopoulos. This occurrence is more likely in cases of small univesicular cysts.

The rupture of echinococcus cysts of the liver into the bile ducts exposes the patient to great dangers because of the complications which may arise. The most frequent of these are: secondary suppuration of the cyst[6], cholangitis and hepatitis, often with the formation of the multiple abscesses[6,8]. Among these complications Dévé also numbers the secondary rupture of the cysts into the pleura and the bronchi. This complication was found in our first case.

The prognosis in cases of rupture of echinococcus cysts of the liver was and still is serious in view of the great percentage of deaths. Although not in possession of recent statistics we believe that for several reasons prognosis is more favorable today. These are due in the main to: the timely diagnosis and operative intervention, the improvement of operative technic, the large scale application of modern means of intravenous hydration, electrolyte balance maintenance, correction of nutritional deficiency states and improved technics of anesthesia. Finally the administration of antibiotics and special Vitamins, such as C and K have largely contributed to a better prognosis and decrease in mortality. The uneventful postoperative course and the quick recovery of the two last mentioned cases in our series have partly encouraged us in our optimistic view.

Diagnosis and Treatment

As to the question of diagnosis, some variability is to be anticipated. In regions where the echinococcus disease is widespread, diagnosis is facilitated by the awareness of the disease by physicians. Furthermore, in those patients in whom an echinococcus cyst has already been diagnosed or who have already been operated upon for echinococcus cyst of the liver or other organ, the appearance of the characteristic symptoms make a correct diagnosis easier. In cases in which the symptoms of a ruptured liver echinococcus cyst appear as the first manifestation of the disease, the diagnosis presents several difficulties owing to the similarity these symptoms bear to those of other diseases, above all cholelithiasis[6].

We share Dévé's opinion that the older view of Lecène and Mondor[12], according to which, "The diagnosis of a ruptured liver echinococcus cyst into the bile ducts is almost impossible", is an overstatement, which can only be explained by the existing lack of diagnostic experience in this disease.

Differential diagnosis is aided by a number of clinical points which make it possible to distinguish a rupture of echinococcus cyst of the liver from other diseases mainly from cholelithiasis[6,10]. The discovery of membranous fragments or daughter cysts in the stools or more rarely in the vomitus is almost a pathognomonic sign.

Membranes are more easily discovered if the stools are washed under water within a fine sieve which will retain any membranes or daughter cysts that may be present. In certain cases hooklets of scolices may be looked for in the duodenal contents aspirated by means of an Einhorn tube[2,18]. X-ray examination may be helpful in certain cases disclosing, instead of gallstone shadows in the region of the gallbladder, an elevation of the diaphragm or a restricted mobility of the latter[10]. Roentgen examination at times may reveal the typical picture of a calcified echinococcus cyst or the existence of gases within the remaining cavity[6,18,22]. Cholecystography or cholangiography may be useful in certain cases.

An important diagnostic aid is offered by laboratory examinations in particular by the specific biological reactions. Thus the increase of eosinophile cells from the normal 2 per cent to 7 to 10 per cent and even 30 per cent is fairly frequent[6,18]. In one of our cases, (third case), the amount of eosinophile cells was 39 per cent. Immunological reactions such as the intradermal test of Casoni and complement-fixation test of Lorenz-Weinberg are positive in a high percentage of cases.

Treatment

We believe that the old dogmatic conceptions of French authors (i.e. Quenu, Duval, Lecène, Mondor) as well as of Argentine and Uruguayian doctors (i.e. Finochietto, Allende, Rodriquez, Prat, Piquerez) have been disproved. Of these the former insisted on the opening, clearing and drainage, merely of the common bile duct while the latter, on the contrary insisted on finding the cyst by any means, and on its subsequent evacuation and drainage.

Medical experience of many centuries has taught us that dogmatic views do not carry weight in every instance, and that often they are even dangerous. With the lapse of time and increased experience, views held to be correct even a short while ago are often proved to be false while other views diametrically opposed take their place. It would take very much of our limited time if we were to go into the views and conceptions held at various times concerning the best operative procedure in case of a ruptured echinococcus cyst of the liver into the bile ducts. We shall therefore confine ourselves to an examination of the views which prevail in the main among Greek surgeons today.

Both the simple opening and drainage of the ruptured echinococcus cyst as well as the common bile duct, if carried out as an emergency measure, may yield satisfactory results. The combination, however, of both procedures, if

possible, undoubtedly constitutes the safest and most satisfactory solution in cases of obstruction of the common bile duct. We shall of necessity limit our surgical intervention to opening and draining the common bile duct, in cases where the ruptured cyst cannot be discovered because it is located within the parenchyma of the liver, and its having collapsed upon rupture. The same procedure must be applied where the serious state of the patient prohibits a prolonged operation.

It is worth mentioning that there are instances in which the ruptured cyst can be drained through the opened and drained common bile duct. In all other cases the echinococcus cyst must be opened and drained. This we consider essential as a recurrence of obstruction is likely to be caused by any membranes remaining within an unopened cyst. This view, moreover, is in accordance with the general rule with surgical practice which demands that all attempts should tend towards eradicating the principal source of the disease. At any rate, it rests with the discretion of the surgeon to decide which procedure is to be followed in a particular instance. If during operation an obstruction of the common bile duct is established, this will constitute a sure indication for drainage. In cases in which the grave condition of the patient does not permit a search for the common bile duct, drainage may be effected at a later stage provided that the symptoms of the obstruction have not disappeared with the opening and drainage of the cyst. Similarly we may, at a second operation, look for a ruptured cyst when, not having discovered it during the first operation, we were forced to content ourselves with draining the common bile duct.

Summary

The subject of rupture of echinococcus cyst of the liver into the bile ducts is reviewed. References are made to cases that have so far been observed in Greece in conjunction with a detailed account of four personally observed. Operative treatment is discussed mainly in the light of experiences of Greek surgeons and the most satisfactory procedures are presented. The concensus indicates that in cases of obstruction of the common bile duct, the opening and drainage of both the ruptured echinococcus cyst and the obstructed common bile duct is the most satisfactory procedure.

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VITAMIN U CONCENTRATE THERAPY OF PEPTIC ULCER*†

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In October, 1952, the author reported the results of fresh cabbage juice in the treatment of 100 patients with peptic ulcer[1]. These results indicated that cabbage juice contained an unidentified antipeptic ulcer dietary factor which promoted more rapid healing of peptic ulcers than has commonly occurred in employing the more conventional methods of therapy. In this series of cases, each patient received 1 liter of fresh cabbage juice daily, and no drugs were prescribed except symptomatically. It was stressed that heating or processing of the antiulcer factor, which has been termed Vitamin U, tended to destroy it.

This clinical study which tested the therapeutic effect of Vitamin U on patients with known peptic ulcers was based on the results of a long series of animal experiments which indicated that experimentally produced peptic ulcers in animals was, in part at least, a nutritional deficiency disorder[2-5]. In recent reports it was pointed out that this factor seemed to be of the nature of a vitamin; that it was contained in a wide variety of green vegetables and also in certain other fresh foods including milk and raw eggs[4,6].

The present study reports an additional series of 100 patients with peptic ulcer which have been treated with Vitamin U therapy. In this series of cases, however, the Vitamin U has been administered in the form of a small volume concentrate prepared from fresh cabbage juice which has made it more acceptable to the majority of patients. The results obtained in this series of cases will be compared to those found in the original 100 cases treated with raw juice and to other series of cases treated by the usual standard forms of therapy.

Present Case Studies

A total of 102 patients were included in the present study. One hundred of these patients had a definite clinical diagnosis of peptic ulcer and 2 additional cases are included with gastric ulcers which were ultimately proven to be due to malignant disease. A number of the patients selected had complications present, such as mild degrees of pyloric obstruction, bleeding, pancreatitis, hepatitis, and varying degrees of psychoneurosis.

The usual clinical and laboratory diagnostic studies were carried out for peptic ulcer as outlined in the previous report. In addition, 80 patients also had uropepsin determinations. The present series of cases received a limited type of bland diet which consisted of only heated food. This diet has already

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been described in detail[1,6,7]. They received no routine medications but were allowed symptomatic therapy for abdominal pain and restlessness in the earlier stages of treatment as indicated. Vitamin U concentrate was administered in the equivalent of the usual dose of 1 liter daily. It was kept under refrigeration and ingested ice cold. It was never warmed or heated. Contrary to the method of management in the earlier series of cases, the majority of these patients were treated on an ambulatory status rather than at bed rest in the hospital.

Analysis of 102 Patients

All but 3 of the cases studied were continually under the direct medical supervision of the author. These 3 were cared for by an associate physician who was thoroughly familiar with the method of experimental treatment employed. The 2 patients with carcinoma were treated in exactly the same manner as those patients with peptic ulcer. In each of these cases, malignant disease was suspected at the time treatment was started, but a positive diagnosis was not initially possible from the clinical and x-ray examinations alone. The important findings in each of the 102 cases have been recorded in Tables I-IV.

The age, sex and race of the patients have been analyzed. The average age for the 100 patients with peptic ulcer is 41.36 years. The range in age is from 11 years to 78 years. There were 3 patients under 18 years of age, Cases No. 13, No. 32 and No. 85. There were 69 male patients and 31 female patients. The 21 gastric ulcers were divided between 13 male patients and 8 females. Duodenal ulcers were divided between 53 males and 20 females. Both patients with carcinoma were females. The race distribution was 94, white; 1, Negro; and 5, Chinese.

The total duration of patients' symptoms and the duration of the presenting attack have been recorded. The symptoms had been present for as little as 10 days or as long as 30 years. In the acute attacks, symptoms had been present from 4 days to 5 years as shown in Tables I-IV.

The peptic ulcers were located in the esophagus in 4 cases; the stomach in 21 cases; the duodenum in 73 cases; and the jejunum in 2 cases. As noted, the 2 cases with carcinoma both had lesions in the stomach. The diameter of the ulcer could be measured in 84 cases and is recorded in the tables. It varied from the small size of 0.4 cm. up to 2.5 cm. in diameter for duodenal ulcers and from 0.3 cm. up to 4.5 cm. for gastric ulcers.

The Vitamin U preparation which was administered to each patient was usually between 50 to 60 c.c. in volume, and each dose represented the equivalent of 1 liter of freshly pressed raw cabbage juice which had been concentrated by cold processing. In a few instances, the concentrate represented 2 liters of cabbage juice instead of one. Consequently, this form of concentrate was administered in a dose of 25 to 30 c.c. daily.

The seasonal incidence of peptic ulcer has been noted in the tables because it seemed probable that not only might there be variation in the number of cases observed seasonally but that possibly patients might respond more rapidly to an unknown dietary factor during certain months of the year than during others. Consequently, the month that each patient was placed on the treatment program was recorded. This designation of the month bears no relationship to the onset of the symptoms. The number of cases appearing each month, including the 100 patients originally treated with fresh cabbage juice, is as follows:

January	18	July	11
February	36	August	11
March	19	September	8
April	14	October	22
May	21	November	21
June	13	December	6

If the six fall-winter months are considered to include October through March, 123 cases came under observation during this period. If the spring-summer months are considered to be April through September, 77 cases came under observation during this six months' period.

As it seemed probable that the degree of activity of the patient might have some bearing on the results of therapy, patient activity has been classified in Tables I-IV under three headings. All patients who spent all or the major part of their treatment while in the hospital are listed as "hospital". Patients who were not hospitalized at all or only for a few days and were under treatment at home but were not at work have been designated as "ambulatory". All those patients who continued their normal mode of life and continued their usual work were classified "at work". The 90 patients in whom ulcer craters were demonstrated by x-ray are classified as follows:

Hospital	27 cases
Ambulatory	22 cases
At work	41 cases
Ambulatory and at work	63 cases

Results of Vitamin U Concentrate Therapy

The results of treatment with Vitamin U concentrate are based on the time at which pain relief occurs and on ulcer crater healing time by x-ray. It is recognized that ordinarily pain relief often is symptomatic only and is very variable. In recording the symptomatology of the present group of patients, the day of pain relief has been designated as the day on which the spontaneous appearance of pain no longer occurs. Occasionally, the exact day of relief could not be very accurately determined, but in a surprising number of instances, the patient would volunteer definite positive information on this point. Pain relief is not considered synonymous with the relief of "acid indigestion" which manifests itself so com-

TABLE I

VITAMIN U CONCENTRATE THERAPY IN 4 CASES OF ESOPHAGEAL ULCER

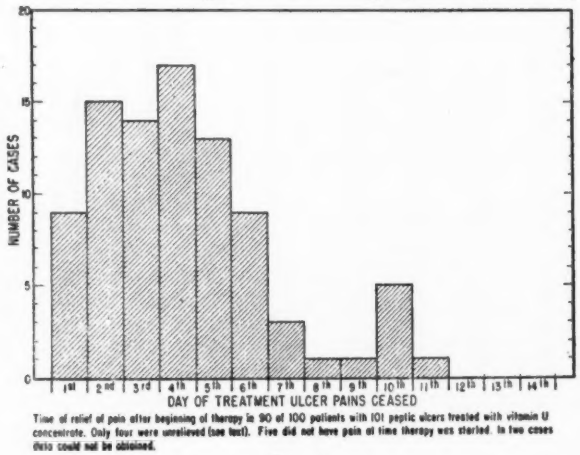
Case No.	Age & Sex	Duration		Peptic Ulcer Location	(By X-ray) Diam. In Cms.	Vitamin U Merck No.	Therapy Month	Patient Activity	Day of Pain Relief	Ulcer Crater Healing Time	Remarks
		Total Illness	Present Attack								
16	69M	4 yrs.	3 mos.	Posterior wall	2.0	52R-3761	Oct.	Ambulatory	10th	10 days	Onset after partial gastrectomy
33	63M	7 yrs.	4 mos.	Anterior wall	1.0	52R-3669	Oct.	At work	3rd	9 days	?Also Meckels peptic ulcer
40	65F	2+ yrs.	2 yrs.	Posterior wall	1.0	51R-6827	Nov.	Ambulatory	2nd	10 days	Esophagoscopic verification
100	41F	3 yrs.	4 mos.	No crater	—	53R-2514	May	Hospital	4th	—	Esophagoscopy—severe peptic esophagitis

TABLE II

VITAMIN U CONCENTRATE THERAPY IN 2 CASES OF JEJUNAL ULCER

Case No.	Age & Sex	Duration		Peptic Ulcer Location	(By X-ray) Diam. In Cms.	Vitamin U Merck No.	Therapy Month	Patient Activity	Day of Pain Relief	Ulcer Crater Healing Time	Remarks
		Total Illness	Present Attack								
77	46M	2 yrs.	2 wks.	?Submarginal	—	53R-1829	Apr.	Hospital	3rd	—	Acute abdominal tenderness subsided
102	48F	16 mos.	3 mos.	Submarginal	0.4	53R-2774	Aug.	At work	?None	14 days	Also Case No. 1. Had gastric resection due to chronic pancreatitis

monly by mild degrees of heartburn and epigastric distress. It should be noted that pain relief in this series has not been produced by any form of medication, and it is the time at which the spontaneous appearance of pain actually ceases. Pain was present in 90 patients with 91 ulcers. In 5 there was no pain. In 4 patients, pain was unrelieved. One of these patients with a gastric ulcer, Case 11, suffered from severe chronic hepatitis. Two others, with penetrating duodenal ulcers, Cases 18 and 31, had a coincident pancreatitis. The fourth case, No. 102, with a jejunal ulcer, suffered from a long-standing chronic pancreatitis which had been identified at the time of a partial gastrectomy which was performed subsequent to her study in this series of patients as Case 1. In Cases 54 and 61, no accurate data relative to pain relief could be obtained. Pain ceased in this group of 90 patients between the first and eleventh days. All but 8 of these were pain-free the first week. These findings are shown graphically in Fig. 1. The average



Time of relief of pain after beginning of therapy in 90 of 100 patients with 101 peptic ulcers treated with vitamin U concentrate. Only four were unrelieved (see text). Five did not have pain at time therapy was started. In two cases data could not be obtained.

Fig. 1

time of pain relief was 4.24 days. Neither of the two patients with gastric carcinoma was relieved.

As there is very little data on when ulcer pain ceases to occur while the patient is not on medicinal therapy or on frequent feedings of food and milk, it is difficult to state whether pain relief in the first week of treatment in 90 per cent of cases is significant in this group of patients or not. Most recently, a group of 20 patients with duodenal ulcer, which was studied on the basis of a double-blind control program which excluded all the time-honored forms of medicinal therapy, showed no cessation of pain during a one to two weeks' period of observation in 18 instances[8]. It should be noted, however, that the great majority of the 100 cases of peptic ulcer studied had previously been under various forms of antiulcer therapy for weeks or for months without any symptom relief.

The use of peptic ulcer crater healing time as shown by x-ray has been described in previous reports[1,7,9-11] and would appear to be the most satisfactory

objective method available at present for the evaluation of improvement in peptic ulcer cases in which craters can unequivocably be demonstrated. This type of therapeutic evaluation has been much more satisfactory for ulcers in the stomach than for peptic ulcers located elsewhere, although it can be applied successfully to a large number of patients with active duodenal ulcer with clearly outlined ulcer craters.

In the 100 patients with peptic ulcer observed, there were 84 cases in which the ulcer craters could be accurately followed by serial x-ray studies. The case distribution of these cases by location is as follows:

Esophageal	3
Gastric	21
Duodenal	59
Jejunal	1

In the 90 cases with peptic ulcer craters demonstrated by x-ray, healing time could only be accurately determined in 80. As the 2 patients with malignant gastric ulcers did not improve, no crater healing time could be determined. The 20 patients with peptic ulcer in which no crater healing time could be determined are recorded in the tables. The reasons for failure may be divided up into those cases in which no crater was demonstrable originally (11 patients); no healing occurred (Case 11 with chronic hepatitis); no satisfactory follow-up studies could be carried out (Cases 27 and 80 with gastric ulcers, and Cases 4, 8, 41, 48 and 61 with duodenal ulcers); and the omission of one case, No. 75, with a huge gastric ulcer. There were 6 cases of gastric ulcer in which crater healing time could not be determined. Case 11, as already noted, was complicated by a severe chronic hepatitis with an exacerbation of acute hepatitis. Case 27 did not have an accurate follow-up but subsequently healed completely. Cases 71 and 88 had gastric carcinoma. Case 75 had such a huge gastric ulcer that it was not included in the average statistics. Case 80 died of a coronary artery occlusion before follow-up studies could be carried out.

There were 14 cases of duodenal ulcer in which crater healing time could not be determined. In 9, this was because no ulcer crater was constantly demonstrated, and in 5, adequate follow-up studies could not be obtained. In one case of jejunal ulcer, No. 77, and in one case of esophageal ulcer, No. 100, the ulcer craters could not be satisfactorily demonstrated.

Ordinarily, repeat x-ray examinations in this series of cases were carried out at 7 to 14 day intervals in order to obtain as exact a crater healing time as possible. In a few cases, the follow-up x-rays were taken at longer intervals. Under this condition, if the ulcer crater had healed, the exact crater healing time might well have been at a shorter interval, but the period of the longer interval had to be designated as "peptic ulcer crater healing time". Also in 3 patients, Vitamin U therapy ceased before the final determining x-ray was taken so that healing

TABLE III

VITAMIN U CONCENTRATE THERAPY IN 23 CASES OF GASTRIC ULCER

Case No.	Age & Sex	Duration		Peptic Ulcer Location	(By X-ray) Diam. In Cms.	Vitamin U Merck No.	Therapy Month	Patient Activity	Day of Pain Relief	Ulcer Crater Healing Time	Remarks
		Total Illness	Present Attack								
3	37M	6 yrs.	6 wks.	Prepyloric	0.8	51R-2822	June	Hospital	2nd	10 days	Well 32 mos. later
7	35M	12 yrs.	1 mo.	Pylorus	1.2	51R-6027	Jan.	Hospital	1st	20 days	Well 24 mos. later
9A	40M	1 yr.	1 mo.	Prepyloric	0.3	51R-6827	Feb.	At work	1st	12 days	Well 24 mos. later
11	60M	22 yrs.	1 mo.	Hi<Curvature	1.5	52R-1485A	Apr.	Hospital	2nd	>24 days	Severe hepatitis
12	51M	6+ yrs.	?	<Curvature	1.5	52R-1485A	Apr.	Hospital	1st	11 days	No recurrence
19	69F	1+ yrs.	6 wks.	>Curvature	1.0	52R-3477	July	Ambulatory	2nd	12 days	Relapse in 1 mo.
21	29F	6 wks.	6 wks.	Mid<Curvature	0.6	52R-3477	Aug.	Ambulatory	no pain	22 days	Severe psycho-neurosis
25	38M	18 yrs.	2 mos.	Pylorus	0.6	52R-3669	Sept.	At work	no pain	17 days	No interval x-ray
27	48M	10 days	10 days	Mid<Curvature	1.5	52R-3761 52R-3669	Oct.	At work	no pain	>24 days	Crater healed 12 days later w/cab. juice
29	48M	3 yrs.	6 mos.	<Curvature	1.5	52R-3761	Oct.	Hospital	2nd	16 days	Crater 0.6 cm. on 6th day
37	42M	9 yrs.	2 mos.	Antrum	0.5	52R-3669	Oct.	Ambulatory	3rd	18 days	No therapy last 7 days
42	44F	7 yrs.	2 wks.	Pyloric canal	0.8	52R-3669 52R-5994	Nov.	Ambulatory	5th	27 days	Marked antral gastritis
52A	59M	12 days	12 days	Prepyloric	0.5	52R-6956	Jan.	Hospital	3rd	18 days	Moderate anemia
B				Pars media	4.6	52R-6956	Jan.	Ambulatory	3rd	54 days	

56	55F	11 mos.	2 mos.	Mid<Curvature	0.5	52R-6711	Jan.	Ambulatory	4th	9 days	
69	49M	18 yrs.	1 mo.	Pylorus	0.6	53R-621	Feb.	At work	4th	18 days	Slight neurosis
71	51F	11 yrs.	1 wk.	>Curvature	1.1	52R-7004	Feb.	Hospital	None	>12 days	Operation showed carcinoma
75	49F	7 yrs.	10 days	<Curvature	2.5	53R-314	Mar.	Ambulatory	5th	63 days	
80	78F	1+ mo.	1 mo.	Mid<Curvature	2.2x1.2	53R-1729	Apr.	Ambulatory	6th	—	Died coronary occlusion 8th day of therapy
82A	53M	19 yrs.	2+ wks.	Pylorus	1.0x0.6	53R-1729 53R-1588	Apr.	At work	26th*	14 days	Broker, works long hours under tension
82B				Hi<Curvature	2.5x1.5	53R-1859 53R-2514				62 days	
83	40F	7 yrs.	3 mos.	Hi<Curvature	2.1x0.8	53R-1588 53R-1859	Apr.	Ambulatory	5th	18 days	Also chronic gastritis. No interval x-ray
88	44F	1 yr.	1 yr.	Mid<Curvature	2.6x2.0	53R-1859	May	Hospital	No Relief	—	Operation showed carcinoma
89	38F	10 mos.	1 mo.	Hi<Curvature	1.2x0.5	53R-1859	May	At work	3rd	19 days	Also alcoholism No interval x-ray
97	48M	15 yrs.	3 mos.	Mid<Curvature	1.5x0.3	53R-1859	July	Hospital	5th	20 days	2mm. irregularity persisted. Subsequent complete healing

*Partial pain relief on 6th day.

TABLE IV

VITAMIN U CONCENTRATE THERAPY IN 73 CASES OF DUODENAL ULCER

Case No.	Age & Sex	Duration		Peptic Ulcer Location	(By X-ray) Diam. In Cms.	Vitamin U Merck No.	Therapy Month	Patient Activity	Day of Pain Relief	Ulcer Crater Healing Time	Remarks
		Total Illness	Present Attack								
1	48F	2 yrs.	2 wks.	Distal cap	0.5	51R-2822	May	Hospital	7th	9 days	Also gallstones
2	51M	8 yrs.	2 wks.	Cap	0.5	51R-2822	May	Hospital	4th	8 days	Well 12 mos. later
4	32M	6 wks.	6 wks.	Cap	0.3	51R-3481	June	Ambulatory	2nd	> 8 days	Also ACTH for hives
5	38M	12 yrs.	1 mo.	Distal cap	0.7	51R-3481	Oct.	Hospital	3rd	9 days	No follow-up
6	27M	3 yrs.	2 mos.	Superior cap	0.3	51R-3482	Dec.	At work	1st	10 days	No follow-up
8	45M	1+ yrs.	1 yr.	Cap	0.5	51R-6027	Feb.	Hospital	3rd	24 days	Crater unchanged 9th day
9B	40M	1 yr.	3 wks.	Bulb	0.5	51R-6827	Feb.	At work	1st	12 days	Also gastric ulcer
10	62M	2 yrs.	1 wk.	Cap	1.0	52R-1485A	Apr.	Hospital	4th	10 days	Advanced arterio-sclerosis
13	11M	2 wks.	2 wks.	Cap	1.2	52R-1485A	Apr.	Ambulatory	5th	10 days	Active school boy
15	58F	8 yrs.	7 mos.	Mid cap	0.3	52R-1485A	May	Hospital	3rd	8 days	Well 12 mos. later
17	47M	15 yrs.	2 yrs.	Apex cap	0.3	51R-6827	July	Hospital	4th	8 days	Cap returned to norm.
18	65M	30 yrs.	1 mo.	Superior cap	0.4	51R-6827	Nov.	Hospital	—	>10 days	Also pancreatitis
20	37M		8 mos.	Base cap	0.8	52R-3477	Aug.	Hospital	1st	6 days	Also lues
22	52M	6 yrs.	5 mos.	Superior cap		51R-6827	Sept.	At work	4th		No definite crater
23	27F	5 yrs.	1 mo.	Bulb	0.4	52R-3477	Aug.	At work	4th	10 days	Well 15 mos. later
24	62M	2 yrs.	10 days	Apex cap	1.0	52R-3761	Sept.	Ambulatory	2nd	12 days	Frequent relapses

26	44F	2+ yrs.	3 wks.	Base cap	0.5	52R-3761	Oct.	Hospital	3rd	15 days	Onset with pancreatitis
28	38F	1¼ yrs.	1 wk.	Apex cap	1.0	52R-3761	Oct.	Hospital	2nd	8 days	Psychoneurotic
30	47F	7 yrs.	1 mo.	Apex cap	0.8	?	Nov.	Hospital	2nd	11 days	Very little pain
31	73M	5 yrs.	6 wks.	Apex bulb	1.0	52R-3669 52R-5447	Oct.	Hospital & Ambulatory	—	34 days	Severe pancreatitis 2 wks. No therapy last week
32	14M	1 yr.	1 yr.	Cap		52R-3669	Oct.	At school	6th		No crater visualized
34	48M	12 yrs.	3 wks.	Base cap	0.6	52R-3669	Oct.	At work	5th	9 days	Well 3 mos. later
35	33F	2 yrs.	1 mo.	Superior cap	0.7	52R-3669	Oct.	Hospital	3rd	14 days	Also cord tumor
36	62M	7 yrs.	5 mos.	Superior cap	0.6	52R-5994	Nov.	Ambulatory	6th	14 days	Onset with hemorrhage
38	34M	2 yrs.	2 yrs.	Base cap	1.5	52R-3669	Nov.	Hospital	8th	15 days	Marked psychoneurosis
39	27M	10 yrs.	8 mos.	Apex cap	0.6	52R-5994	Nov.	At work	6th	12 days	Moderate psychoneurosis
41	66M	30 yrs.+	15 mos.	Duodenogastric	1.3	51R-6827	Nov.	Ambulatory	4th	>13 days	14th day crater 0.5 cm. Had Bilroth I operation
43	35F	3⅜ yrs.	4 mos.	Apex cap	0.8	52R-5994	Nov.	Hospital	4th	7 days	Relapsed in 6 wks.
44	50F	20 yrs.	6 mos.	Mid cap	0.8	52R-5994	Nov.	Ambulatory	7th	10 days	Relapsed in 3 wks.
45	29M	10 mos.	3 mos.	Body cap	1.4	52R-5994	Nov.	Hospital	4th	16 days	Severe psychoneurosis
46	24F	1 yr.	1 yr.	Inferior cap	0.5	52R-5994	Nov.	At work	2nd	10 days	Overweight
47	62M	2 yrs.	3 days	Mid cap	0.8	52R-5994	Nov.	Home in bed	2nd	12 days	Onset with pancreatitis

(*Continued on next page*)

TABLE IV (*continued*)

Case No.	Age & Sex	Duration		Peptic Ulcer Location	(By X-ray) Diam. In Cms.	Vitamin U Merck No.	Therapy Month	Patient Activity	Day of Pain Relief	Ulcer Crater Healing Time	Remarks
		Total Illness	Present Attack								
48	54M	1+ yrs.	6 mos.	Base cap	1.3	52R-5994	Nov.	Hospital	5th	>15 days	X-ray negative 1 mo. after treatment
49	40F	16 yrs.	10 wks.	Mid cap	0.8	52R-6030	Nov.	At work	1st	21 days	Overweight
50	47F	18 mos.	6 mos.	Inferior cap	0.5	52R-6710	Dec.	At work	3rd	16 days	
51	50M	15 yrs.	5 days	No crater	—	53R-6856	Jan.	Hospital	2nd	—	Hematemesis at onset
53	66F	14 mos.	2 mos.	Anterior cap	1.0	52R-6710	Jan.	At work	1st	22 days	Late follow-up x-ray
54	35F	3½ yrs.	2 wks.	No crater	—	52R-6848	Jan.	At work	—	—	No follow-up
55	45M	22 yrs.	6 wks.	No crater	—	52R-6711	Jan.	At work	10th	—	X-ray 11th day "Normal duodenum"
57	36M	18 mos.	1 mo.	Bulb	0.4	52R-186	Jan.	Ambulatory	8th	16 days	Also acute hepatitis
58	40F	3½ yrs.	3 mos.	Central bulb	0.5	52R-6956	Jan.	At work	9th	11 days	
59	49M	3 wks.	3 wks.	Post bulbar	0.6	53R-186	Feb.	At work	5th	11 days	Very little pain
60	48M	8 yrs.	2 mos.	Bulb	1.5	53R-186	Jan.	Hospital	3rd	12 days	
61	54M	16 yrs.	3 mos.	Posterior cap	2.5	53R-186	Jan.	Hospital		>24 days	Operated. No follow-up
62	51M	4 yrs.	2 wks.	Base cap	0.7	52R-6847	Feb.	Ambulatory	5th	8 days	Moderate psycho-neurosis
63	53M	30 yrs.	3 wks.	Base bulb	1.1	52R-6847	Feb.	At work	11th	25 days	Pancreatic-calcification

64	49M	20 yrs.	6 wks.	Inferior base cap	1.3	52R-6711	Feb.	Ambulatory	4th	18 days	Moderate psychoneurosis
65	41F	10 mos.	3 wks.	Inferior base cap	1.0	52R-7004	Feb.	At work	No pain	18 days	Recent cholecystectomy
66	30M	1 yr.	1 mo.	Mid bulb	0.7	53R-621	Feb.	At work	2nd	20 days	
67	27M	1 mo.	1 mo.	Central bulb	0.4	53R-621	Feb.	At work	4th	20 days	First attack
68	28M	2¾ yrs.	6 wks.	Apex cap	1.2	52R-7004	Feb.	Ambulatory	6th	9 days	
70	34M	2 yrs.	2 mos.	Cap	0.5	53R-621	Feb.	At work	6th	23 days	Neurosis marked
72	62M	4 yrs.	1 mo.	Apex bulb	1.2	53R-856	Mar.	Ambulatory	6th	9 days	Melena at onset plus anemia
73	33F	4 yrs.	4 days	Base cap	1.0	53R-856	Mar.	Hospital	6th	15 days	Severe psychoneurosis
74	54M	25 yrs.	1 mo.	Post bulbar	0.5	53R-856	Mar.	At work	3rd	9 days	slight anemia
76	29M	16 yrs.	6 mos.	Cap and postbulbar duodenitis	—	53R-1729	Mar.	Ambulatory	3rd	—	After 10 days' therapy —"normal bulb and postduodenum"
78	31M	10 yrs.	6+ mos.	Bulbar or postbulbar	0.5	53R-1627	Apr.	At work	4th	14 days	Relapse in 2 mos.
79	60M	27 yrs.	1 wk.	Posterior bulb	0.8	53R-1627	Apr.	Hospital	4th	18 days	Also coronary disease
81	33M	5 yrs.	3 wks.	Mid bulb	1.0	53R-1627	Apr.	Hospital	2nd	15 days	Also mitral valvulitis
84	58M	20 yrs.	7 wks.	Deformed, tender irritable bulb	—	53R-1859	Apr.	At work	10th	—	After 16 days' therapy x-ray—only deformity, bulb
85	17M	3 mos.	3 mos.	Central cap	0.7	53R-1859	Apr.	At work	4th	13 days	Bizarre history
86	29M	6 yrs.	3 mos.	Mid bulb	1.0	53R-2328	June	Ambulatory	5th	14 days	Residual bulb depression persists

(*Continued on next page*)

TABLE IV (*continued*)

Case No.	Age & Sex	Duration		Peptic Ulcer Location	(By X-ray) Diam. In Cms.	Vitamin U Merck No.	Therapy Month	Patient Activity	Day of Pain Relief	Ulcer Crater Healing Time	Remarks
		Total Illness	Present Attack								
87	25F	2 yrs.	3+ mos.	Extremely irritable eccentric cap	—	53R-1859 53R-2514	May	At work	16th*	—	Eats Chinese food only
90	45M	2 yrs.	6 mos.	Superior cap	0.5	53R-2514	May	At work	4th	14 days	Final x-ray—"only minimal deformity" cap
91	30F	5 yrs.	5 wks.	Posterior inferior cap	0.4	53R-2328	May	Ambulatory	5th	14 days	Also ulcerative colitis
92	74M	6 yrs.	2 wks.	Posterior cap	1.0	53R-2328	June	Ambulatory	7th	13 days	Also Case No. 31
93	41M	17 yrs.	3 wks.	Posterior cap	0.7	53R-2514	June	At work	5th	14 days	Residual bulb depression persists Also Case No. 49
94	52M	8 yrs.	3 wks.	Mid posterior cap	1.0	53R-2776	June	At work	8th	20 days	No interval x-ray
95	54M	30 yrs.	15 mos.	Irritability & spasm cap	—	53R-2776	June	At work	10th	—	Psychoneurotic, tense, nervous hypochondriacal
96	52M	5 yrs.	5 yrs.	Apex cap	0.5	53R-2776	June	At work	10th	19 days	No interval x-ray
98	48F	5 yrs.	4 days	Apex cap	0.4	53R-3261	July	Ambulatory	1st	10 days	Convalescing from hysterectomy
99	73M	15 mos.	3 wks.	Base bulb	0.6	53R-2776	July	Hospital	No pain	10 days	Had severe hemorrhage
101	40M	7 yrs.	1 mo.	Base cap	0.5	53R-2774 53R-2775	Aug.	At work	2nd	11 days	Also amebic dysentery

*Partial pain relief on 6th day.

time did not accurately reflect the period of treatment. These unusual circumstances are recorded in the tables of crater healing time under "Remarks".

Interpretation of Findings

Age, Sex and Race:—Age, sex and race seemed to have no bearing on the effect of therapy with Vitamin U. The patients were divided into two groups in order to determine whether ulcers in older patients might heal more slowly than those in younger patients. The first group included all patients 41 years of age and younger, and the second group included all patients over 41 years of age. There were 36 patients in the first group, and their ulcer crater healing time was 14 days. There were 44 patients in the second group, and their ulcer crater healing time was 12.2 days.

Duration of Illness:—A study of the total duration of symptoms indicated that the length of a patient's illness had very little, if any, effect on the healing time of his ulcers as demonstrated by x-ray. In order to determine this, the patients were divided into four groups relative to the length of the history. The number of cases in each of these groups and their ulcer crater healing times are as follows:

TABLE V

Total Illness	No. of Cases	Crater Healing Time in Days
Less than 2 months	5	16.2
2 Months to 1 year	8	14.25
More than 1 year to 10 years	49	13.2
More than 10 years to 30 years	15	15.9
Total	77	14.3

Location and Size of Ulcers:—As already noted, an ulcer located in the first part of the duodenum tends to heal a little more rapidly than one located in the stomach. Peptic ulcers on the lesser curvature of the stomach, particularly those near the angulus where they are inclined to be of large size, heal more slowly than those in the pylorus and antrum. Ulcers in the esophagus tend to heal rapidly if the observations of the short crater healing time in only 3 cases (Cases 16, 33 and 40) are a correct indication. If a peptic ulcer forms in the jejunum, it may heal rapidly but there is insufficient data in studying 2 cases (Cases 77 and 102) to properly judge the effect of location on the healing of a jejunal lesion.

In an attempt to analyze the relationship between the size (diameter) of a peptic ulcer and the rate of healing, ulcers have been divided into two major groups. All ulcers of average size or smaller were placed in the first group and

designated as small ulcers, and all ulcers greater than average size were placed in the second group and designated as large ulcers. These averages were based on a study of 130 cases of peptic ulcer with clearly defined craters which were encountered in the series of cases treated with raw cabbage juice[12] and in the present series. There were 35 cases of gastric ulcer with an average diameter of 0.983 cm. (1.0 cm.); and 95 cases of duodenal ulcer with an average diameter of 0.712 cm. (0.7 cm.). Three cases of gastric ulcer, Nos. 52B, 75, and 82B were so large they were designated as "huge ulcers" and not included in the general classification of small and large. These ulcers were 2.5 cm. in diameter or larger (see Table III). Seventy-nine of the 130 cases were treated with Vitamin U concentrate and could be followed by crater healing time determinations. Under this classification there were:

	Small	*Large*	*Huge*
Gastric ulcer	10	7	3
Duodenal ulcer	35	24	–

The ulcer crater healing time for these three groups of ulcer cases was:

	Small	*Large*	*Huge*
Gastric ulcer	16.5 days	16.6 days	59.7 days
Duodenal ulcer	12.8 days	14.9 days	—

If 14 additional cases of gastric ulcer and 36 additional cases of duodenal ulcer which received raw cabbage juice are added to this analysis, the comparative crater healing times are as follows:

	Small	*Large*	*Huge*
Gastric ulcer	13.75 days	17.3 days	59.7 days
Duodenal ulcer	13.25 days	13.59 days	—

Actually the size of a peptic ulcer, when represented by measurements of the diameter, except for the huge type of gastric ulcer, seems to have very little effect on the rate of ulcer crater healing when Vitamin U is administered. Ulcer depth or penetration measurements might prove more informative in calculating the rate of ulcer crater healing, but accurate determinations of the depth of most duodenal lesions are almost impossible to obtain by the present technical methods which are employed.

Seasonal Variations:—In considering a possible effect of the season of the year on the healing time of ulcer craters, the time was calculated for each month of the year jointly for both series of 100 cases as follows:

	Jan.	*Feb.*	*Mar.*	*Apr.*	*May*	*June*	*July*	*Aug.*	*Sept.*	*Oct.*	*Nov.*	*Dec.*
No. of cases	10	23	10	9	16	9	9	8	6	17	15	2
Crater healing time	17.9	17.1	15.1	13.7	9.9	13.7	11.9	13.3	14.5	13.8	11.9	13.0

The variation from a healing time of 10 days in May to 18 days in January may not be significant because of the small number of cases involved, but when the figures for the 6 months fall-winter and spring-summer periods are contrasted, there appears to be a tendency for ulcers to respond to therapy more rapidly in the second period. The average crater healing time for the fall-winter period is 14.9 days and for the spring-summer period is 12.4 days. Disregarding other factors which may influence peptic ulcer crater healing time, this difference of 2.5 days might be related to the finding that spring and summer varieties of cabbage have a higher antiulcer factor content than fall and winter ones[5]. Although the cabbage juice concentrates were not always used immediately after their preparation, they were usually administered within a few weeks.

Potency of Concentrate:—Certain preparations of Vitamin U concentrate might well be less effective in treatment because of inferior source material, defective preparation or unsatisfactory storage conditions. Such deficiencies might be suspected rather than real.

In studying the effect of the various aliquots of Vitamin U on the healing of peptic ulcers, it was found there were three which may have been lacking in satisfactory concentration of Vitamin U (Tables I-IV). In nearly all cases treated with these three aliquots, a patient received the equivalent in concentrate of 1 liter of juice daily for the period of treatment. One of the lots suspected of being inferior, #53R-450, was stored at room temperature for a period of 3 weeks before it was refrigerated, but storage under these conditions may not have had any effect on its potency. A second lot, #53R-1859, was flavored with a new chemical substance which was not palatable, occasionally caused nausea, and was probably responsible for the suspected inferiority of the product. The third lot, #53R-5765, was a concentrate which was supplied in only a small amount and may or may not have been entirely satisfactory. It was unusually dark in color.

Until satisfactory methods of laboratory standardization of cabbage juice concentrate become available, the results of assay on human subjects will remain the chief indication of the potency of the product.

Patient Activity:—The activity of patients had, as a rule, little effect on the improvement of their peptic ulcers. Those patients who were hospitalized for the majority of their treatment were apparently relieved slightly more rapidly than the more active ones. This seemed particularly true for large gastric ulcers.

An analysis of 76 cases of gastric and duodenal ulcer in the present series of patients reveals differences in ulcer crater healing time relative to patient activity as follows:

TABLE VI

Degree of Activity	No. of Cases	Crater Healing Time
Gastric Ulcer:		
1. Hospital	6	15.8 days
2. Ambulatory	6	17.7 days
3. At work	5	16 days
4. Ambulatory and at work	11	16.9 days
Duodenal Ulcer:		
1. Hospital	21	11.9 days
2. Ambulatory	14	13.8 days
3. At work	24	15 days
4. Ambulatory and at work	38	14 days

When 17 patients with gastric ulcer and 36 patients with duodenal ulcer which had been treated with fresh cabbage juice are added to this series, an analysis of the combined groups is as follows:

TABLE VII

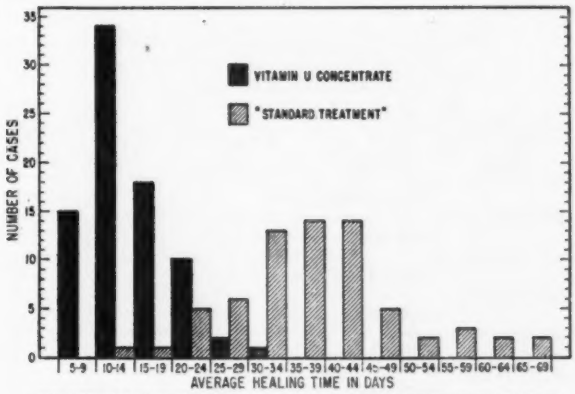
Degree of Activity	No. of Cases	Crater Healing Time
Gastric Ulcer:		
1. Hospital	19	13.5 days
2. Ambulatory	9	18 days
3. At work	6	15.3 days
4. Ambulatory and at work	15	17.5 days
Duodenal ulcer:		
1. Hospital	47	11.9 days
2. Ambulatory	18	14.8 days
3. At work	30	16.4 days
4. Ambulatory and at work	48	15.8 days

In comparing the hospitalized cases to the active cases in the group of 34 gastric ulcers and in the group of 95 duodenal ulcers, it is evident that the average patient who is hospitalized for treatment the ulcer heals four days sooner than in the non-hospitalized patient. It must be taken into account in interpreting these results that at first nearly all cases with ulceration were put to bed and only

selected mild cases were permitted to be up and about. Later on all cases were treated on an ambulatory status except those severely ill and a few others from out of town who did not actually require confinement to bed. This change in patient management led to many more of the less severe cases being treated while active.

Comparison of Vitamin U Therapy With Other Methods of Treatment

The therapeutic effect of Vitamin U concentrate when compared to raw cabbage juice appears to be the same. Pain ceased on the average in 4.24 days in patients receiving the concentrate as compared to 3.92 days in patients receiving the raw juice. If the incidence of pain relief shown in Fig. 1 is compared with a similar chart for cabbage juice therapy[1], they appear comparable in effectiveness. A comparison of ulcer crater healing time for the two series of cases shows very similar results. These are recorded in Table VIII. For the 80 cases receiving



Crater healing time in 79 cases with 80 peptic ulcers treated with vitamin U concentrate, compared with healing time in 68 cases (reported in the literature) in which "standard treatment" was given.

Fig. 2

the concentrate, the average crater healing time was 13.5 days, and for 54 cases of all types receiving raw juice, the average crater healing time was 13.1. Using cessation of pain and ulcer crater healing time as criteria for recovery, it would appear that there was no demonstrable difference between the therapeutic effect of the raw juice and of the concentrate.

When Vitamin U therapy is compared to the usually accepted forms of "standard" therapy which include frequent feedings of a bland diet, antacids, sedatives, and antispasmodics, it appears that Vitamin U therapy promotes a more rapid recovery. Fig. 2 compares ulcer crater healing time in 84 patients receiving Vitamin U concentrate with a group of 68 patients taken from the literature[9] on "standard" therapy which contains 6 cases of gastric ulcer and 62 of duodenal ulcer. The increased rate of healing time in the patients receiving Vitamin U is strikingly demonstrated. This same type of graphic chart has been recorded in the publication on cabbage juice therapy[1] and shows a similar result.

If we compare ulcer crater healing times in patients treated with Vitamin U concentrate to a collection of all the cases recorded in the literature[1,7,9-19] which have received "standard" forms of treatment, nearly always under the condition of hospitalization, an improved rate of healing in a ratio of about 3 to 1 is noted. This is recorded in Table IX. When all types of ulcer are compared, 134 cases treated with Vitamin U showed an average crater healing time of 13.4 days, and 295 cases on the "standard" form of therapy showed ulcer crater healing time of 49.9 days. The differences in crater healing time shown in Table IX are so clear-cut they appear to be statistically valid.

There are very few types of recently introduced specific drug therapy in which ulcer crater healing time has been determined. In two series of cases receiving Banthine Bromide, a rapid duodenal crater healing time was reported in 18 in one series[12], and in the second, duodenal ulcer crater healing time was

TABLE VIII

AVERAGE CRATER HEALING TIME OF PEPTIC ULCERS TREATED WITH VITAMIN U AS (1) A CABBAGE JUICE CONCENTRATE AND AS (2) RAW CABBAGE JUICE.

TYPE OF ULCER	TYPE OF THERAPY	NUMBER OF CASES	CRATER HEALING TIME IN DAYS
GASTRIC	CONCENTRATE	17	16.3
	RAW JUICE	17	14.0
DUODENAL	CONCENTRATE	59	12.9
	RAW JUICE	36	13.0
ALL TYPES*	CONCENTRATE	80	13.5
	RAW JUICE	54	13.1

*Including Esophogeal and Jejunal.

delayed beyond 6 to 8 weeks in 28 of 71 cases[13]. In a large series of cases receiving "around-the-clock" alkalinization, excellent results have been reported.

The Significance of Vitamin U Therapy

The therapeutic results of Vitamin U therapy of peptic ulcer which have been presented in this report indicate that this disease is fundamentally a disorder of nutrition. Apparently, some factor is lacking in a patient's diet which leads to the development of peptic ulceration of the gastrointestinal mucosa and which will correct this lesion when it is fed in adequate amounts. Numerous chick and guinea pig experiments support this assumption[3,5]. The exact nature of the dietary deficiency is not yet known. The antiulcer factor involved is readily destroyed by heat and may be rapidly destroyed by oxidation processes as well. This factor has properties suggesting that it is a vitamin and has tentatively been termed Vitamin U (antiulcer vitamin), although its final identification may alter the vitamin concept.

Its mode of action is not known. It has been postulated that Vitamin U, or some fraction or derivative thereof, increases the resistance of the mucosal lining of the esophagus, stomach and intestine to the erosive and ulcerating action of gastric juice which is high in acid content and rich in pepsin. If a patient is markedly deficient in the antiulcer factor, he might readily develop ulceration when the acid-pepsin content of his gastric juice was low. This concept would readily explain the low gastric acidity and uropepsin flow so often encountered in individuals with large gastric ulcers.

It is possible that some obscure defect in liver function may interfere with the normal utilization of Vitamin U in a fashion similar to that involved with Vitamin K and Vitamin A metabolism. The development of cincophen gastric ulcers in laboratory animals and in man suggests this[2,3]. It is noteworthy in this respect that Case 11 with a very severe hepatitis is the only case in the entire

TABLE IX

AVERAGE CRATER HEALING TIME OF PEPTIC ULCERS TREATED WITH VITAMIN U COMPARED TO "STANDARD" FORMS OF TREATMENT RECORDED IN THE LITERATURE.

TYPE OF ULCER	TYPE OF THERAPY	NUMBER OF CASES	CRATER HEALING TIME IN DAYS
GASTRIC	VITAMIN U	34	15.1
	STANDARD	76	43.8
DUODENAL	VITAMIN U	95	12.96
	STANDARD	79	36.2
ALL TYPES	VITAMIN U	134	13.4
	STANDARD	295	49.9

series, except those complicated by malignant disease or by pancreatitis, which failed completely to respond to Vitamin U concentrate therapy.

The development of a potent concentrate of raw cabbage juice has not only greatly facilitated the therapeutic use of Vitamin U but has demonstrated that the active principle involved may ultimately be obtained in a yet simpler form. That this is so is exemplified by the recent development of a solid form which has already been administered to 11 patients in capsules. The early results of capsule therapy appear promising.

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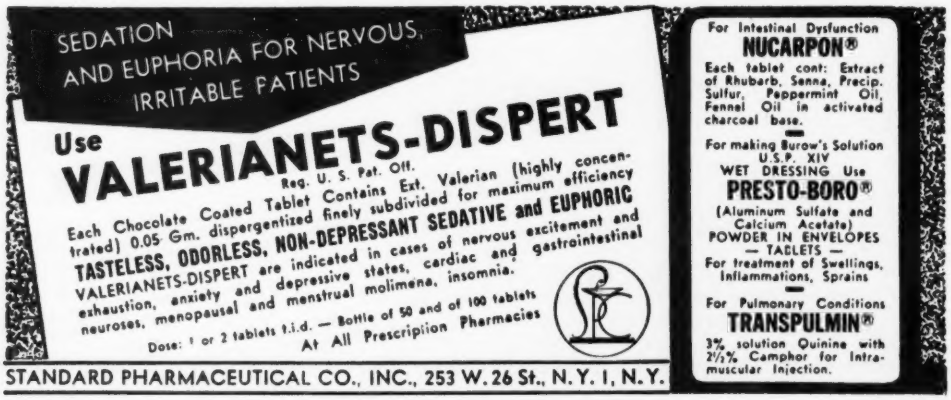

President's Message

What constitutes the specialty of Gastroenterology? That is an all embracing question. Its answer will vary according to who asks the question.

If it is the young graduate of Medical School who is considering the best means of preparing himself to qualify as a Gastroenterologist, he is confronted by a dilemma. Everyone is agreed that a Gastroenterologist should have a thorough background of internal medicine. He should be familiar with x-ray technic and interpretation. When it comes to therapy he will be called upon to select a choice of measures—some medical, some surgical and some roentgenological. How can he secure the best training in this field? He is told he needs two to three years of residency training in internal medicine after he has finished his interneship, with one or two additional years of residency in Gastroenterology. That leaves him no opportunity for training in x-ray, or else he decides to take all his residency in x-ray work.

It would therefore seem obvious that a correlated program of training in Gastroenterology was very much needed. This is one of the problems we hope to study as a primary objective of the American College of Gastroenterology.

Another viewpoint of what constitutes Gastroenterology is the Gastroenterologist who conducts his own x-ray examinations. He feels that accurate diagnosis is the first essential to practicing good Gastroenterology, and this can only be achieved by examining his patient, using clinical, laboratory and x-ray technics to achieve this goal.

Still another viewpoint is that of the internist who feels that the Gastroenterologist should confine his efforts to diagnosis and medical

treatment, and to leave diagnostic procedures of the laboratory and x-ray field to those most competent to use these procedures. He also feels that surgical procedures should be carried out by competent surgeons in the field of Gastroenterology. It would appear therefore that there is no agreement as to the exact definition of what constitutes the specialty of Gastroenterology.

Gastroenterology was one of the first specialties of medicine to emerge notably after the first World War. Progress and research in Gastroenterology reached such a high degree of proficiency that it appeared to be headed for signal distinction. What has happened in the past two decades to reverse this trend? I believe the answer to this question lies in the vast improvements in technic and the far-reaching importance of allied advances in therapy and diagnosis in this field. The field has become all embracing so that we have divisions of Gastroenterology to the point where we have a well-developed field of Pediatric Gastroenterological Surgery, to use one illustration.

The challenge presented, therefore, will be one of the objectives of the American College of Gastroenterology—to consolidate and elevate the specialty of Gastroenterology by a careful study in cooperation with all of the allied specialties which have a bearing on this problem.

These are high ideals, but only by recognizing the problems can solutions be found, and it is our sincere hope that will be the aim of the American College of Gastroenterology.

Sigurd W. Johnson

EDITORIAL

Gastric and Duodenal Ulcer

Patients who have ulcers and who listen to the radio, watch television or read newspaper articles describing these new preparations and their virtues often become confused, and many patients tell the physician what they would like him to prescribe as a sure cure for their ulcer. Unfortunately, there is nothing certain and nothing specific in any of these magic drugs. The patient still requires mental and physical rest, diet and at times, psychotherapy in addition to the medication.

If anemic he requires liver, iron and vitamins orally or by injection; hemorrhage or melena requires transfusions, Vitamin K, ascorbic acid, C.V.P. capsules, (a citrus flavinoid compound combined with ascorbic acid); persistent vomiting and dehydration calls for infusions of glucose, (500 to 1,000 c.c. in saline). Emetrol (15 c.c.) one-half of one ounce repeated at 15 minute intervals for three doses; a teaspoonful of dramamine by mouth; a suppository of dramamine or nembutal sodium 3 grains, (0.2 gm.) may relieve the nausea and vomiting.

When indicated, duodenal feeding, rectal feeding, milk drip with alkalis or aluminum gel may be used.

For the heartburn and acidity shall the physician prescribe bicarbonate of soda alone, or in combination with calcium carbonate, tribasic calcium or magnesium phosphate, magnesium superoxol, bismuth or magnesium oxide, or should he order one of the aluminum gel combinations, or the anticholinergic drugs in addition to the diet?

Bicarbonate of soda is a rapid neutralizer of gastric acidity. Given in doses of 15 to 30 grains (1 to 2 grams) causes an increased amount of carbon dioxide, and if repeated for any length of time may cause alkalosis. The urine becomes alkaline and at times forms crystalline phosphates in the pelvis of the kidney, ureter and the bladder.

When a patient has taken alkalis to an excess the physician must watch for the initial symptoms of alkalosis: headache, thirst, anorexia, dry mouth, excessive thirst, lassitude, nausea, vomiting, mental disturbances, muscle and joint cramps, dizziness, tingling in the extremities and spasmodic movements. Upon the first appearance of any of these symptoms, alkalis should be completely withdrawn and 60 c.c. (2 ounces) milk and cream given at half hour intervals. Severe vomiting and threatened convulsions require intravenous physiologic saline solution to overcome the loss of chlorides. At times the oral administration of one third of an ounce (10 gm.) of sodium chloride daily may prevent or abort the threatened alkalosis.

Further need to control acidity or for relief of ulcer symptoms, tribasic calcium phosphate and tribasic magnesium phosphate may be given in suitable doses. Prescribe calcium phosphate tribasic 10 to 15 grains (0.6 to 1 gm.); magnesium phosphate tribasic 8 to 10 grains (0.5 to 0.6 gm.) one powder in water every 2 or 3 hours, unless the bowels become too loose. Magnesium superoxol (magnesium perhydrol) may be given in 5 to 10 grain (0.3 to 0.6 gm.) doses as an antacid. The gastric juice converts it into magnesium chloride and hydrogen peroxide. In addition to its antacid action it tends to minimize excessive gastric and intestinal fermentative processes, chronic constipation, and flatulence.

Calcium carbonate given between feedings to ulcer patients is well tolerated and gives complete neutralization of the acidity half hour after its administration. The dose is 30 to 60 grains (2 to 4 gm.).

Tendency to constipation is overcome by giving the patient magnesium oxide in the early part of the day, instead of calcium carbonate, or the two may be combined in one powder: calcium carbonate 10 to 15 grains (0.6 to 1 gm); magnesium oxide ponderosa 10 to 15 grains (0.6 to 1 gm.).

The aluminum preparations, such as Amphojel, Phosphagel, Malcogel, Maalox, Aludrox, Creamalin, Kolantyl-Gel, Carmethose, Gelusil and many others, in liquid or tablet form are useful antacids, neutralizers and adsorbents of the acid, relieve heartburn and pain. These preparations as well as calcium carbonate are not absorbed into the systemic circulation, they do not cause acid rebound in the stomach, and have no effect upon the acid base equilibrium of the body.

In gastritis with or without erosions or ulcer, the physician may prescribe protectants such as the bismuth salts which are insoluble. Bismuth subcarbonate or subgallate 15 to 30 grains (1 to 2 gm.) suspended in water, and given on the emtpy stomach in the morning, having the patient remaining in a prone position, forms a protective covering over the mucosa and ulcer. Bismuth subnitrate has been found to cause irritation and burning in many patients, this being due to the breaking up of the subnitrate radical by the hydrochloric acid to form a nitrite, which acts as an escharotic and irritant. The bismuth salts may be combined with magnesium superoxol, bicarbonate of soda, calcium carbonate, magnesium oxide in various proportions depending upon the patient's requirements.

It is advisable to caution the patient that the stools may assume a dark or black color, and that this is not due to bleeding from the stomach or duodenum.

Mucotin, Trimucolan and similar combinations of aluminum hydroxide gel, magnesium trisilicate and gastric mucin, cling to the stomach wall in the presence of mucus and act as buffering agents. Anion exchange resins alone or combined with hyoscine hydrobromide or belladonna in tablet, capsule or powder (Resinat), or Resmicon in tablet form inactivate pepsin as the result of the acid reduction. Average dose is 1 or 2 capsules or tablets every 2 or 3 hours. These

preparations are as effective as the aluminum preparations, as judged by roentgen and/or gastroscopic studies.

Protein hydrolysates are good buffers and neutralizers like milk and cream, but not satisfactory in marginal ulcer.

For continuous neutralization of the acid, tablets of Nulacin, Parluguan, Almasil, containing milk and antacids have been found useful in ambulatory and bed patients.

Patients may or may not be relieved by the above mentioned substances, and therefore, in addition to the alkalis and protectants require a careful supervised diet, Atropine, Belladonna, Syntropan, Syntrogel, Morphine, Demerol, Dilaudid, Hycodad, or similar pain relievers. Sometimes drugs like extract of hyosciamus, phenobarbital, Lusyn, Butisol, Profenil, Octin, Trasentin, Pavatrine, Bentyl, Mucogel, and Mucogel B, Centrine, Trevidal, Donnatal, Sebella and Bunesia, will act satisfactorily in overcoming restlessness, spasm and pain.

Anticholinergic drugs like Banthine, Pro-banthine, Antrenyl, Co-Elorin, Pamine, Prantal, Tricoloid, Dibutoline, have been found satisfactory as acid repressants and inhibitors of gastric and intestinal motility. Many patients after taking one or the other of the above complain of dryness of the mouth and throat, blurring of vision and urinary disturbances, and should not be prescribed to patients with glaucoma and prostatic hypertrophy.

Patients with intractable pain due to ulcer may be given relief by intramuscular injections of tetraethylammonium three times daily between feedings and at bed time. A preliminary dose of 300 mg. (5 grains), increased to 600 mg. (10 grains), may be tried. Its response is greater than atropine or epinephrine alone or in combination. Failure to give relief may be due to penetration of the ulcer, irritation of the peritoneum or organic obstruction of the pylorus. Tetraethylammonium should be given to patients only when they are hospitalized as untowards symptoms such as weakness or fainting spells may occur after the larger doses.

While urogastrone and enterogastrone have been given a fair trial, they have been found wanting as a cure for ulcer. Antihistaminic preparations also failed to produce the desired results in patients with ulcer symptoms or even in hyperacidity.

Larostidin, Synodal and foreign proteins have been advocated and used with more or less success in the treatment of gastric and duodenal ulcers. After vagotomy, urecholine is being tried to overcome gastric emptying and to restore motility. This drug may be given orally or sublingually in doses from 10 to 30 mg. (⅙ to ½ grain).

Intractable and recurrent ulcers, repeated hemorrhages, perforated ulcers, all require surgical intervention.

SAMUEL WEISS, M.D.

NEWS NOTES

Dinner Tendered Dr. Rene Gutman

On Monday evening, 1 March 1954, the National Gastroenterological Association honored Dr. René Gutmann and his colleague, Dr. Guy Albot of Paris, France, with a dinner at the Lotos Club in New York City.

Dr. Gutmann, an Honorary Fellow of the National Gastroenterological Association, is President of the IVth European and Mediterranean Congress of National Gastroenterological Associations which will meet in Paris, France, 28 June 1954. He and Dr. Albot were in New York City on their way to the Mexican Congress of Gastroenterology.

Attending the dinner were officers of the National Gastroenterological Association: Dr. Sigurd W. Johnsen, President; Dr. A. Xerxes Rossien, Secretary; Dr. Samuel Weiss, Editor and Dr. Anthony Bassler, Honorary President. The New York Chapter was represented by Dr. Harry Barowsky, President; Dr. Frederic W. Bancroft, Vice-President; Dr. Alexander Slanger; Dr. Franz J. Lust and many other members of the Chapter. Representing the New Jersey Chapter were Dr. Louis A. Perkel; Dr. Leo H. Siegel; Dr. Edward Sciorsci and Dr. F. Vogel.

Among the other distinguished guests present were Dr. Asher Winkelstein; Dr. J. Russell Twiss; Dr. Leon T. LeWald; Mr. Jean DeLagarde, French Consul-General and Mr. George Assié of the office of the Cultural Counselor to the French Embassy.

Dr. Roy Upham, Secretary-General of the National Gastroenterological Association was the toastmaster and Dr. William C. Jacobson was in charge of arrangements. Other members of the committee were Dr. Frank A. Cummings, Providence, R. I.; Dr. Harry M. Eberhard, Philadelphia, Pa.; Dr. Harry Barowsky, New York, N. Y. and Dr. Benjamin J. Macchia, Jersey City, N. J.

Following the dinner, Dr. Gutmann spoke on "Early Diagnosis of Malignancy of the Stomach" with lantern slide demonstration.

International Academy of Proctology Meets

All physicians are cordially invited to attend the Sixth Annual Convention of the International Academy of Proctology to be held at the Palmer House, Chicago, Illinois, April 8, 9, 10 and 11th, 1954.

An extensive Motion Picture Seminar of Proctologic Surgery (including office technics) will be held on April 11th, 1954. All scientific papers will present the latest developments in proctology and gastroenterology.

Because general practitioners, as well as gastroenterologists and proctologists, face proctologic problems in their daily practice, much of the program has been planned to answer their questions.

There is no fee for attendance at the Annual Convention of the International Academy of Proctology. These Conventions, as well as all other activities of the Academy, are directed toward the further development of proctology. All physicians interested in proctology are therefore invited and welcomed to the Annual Meeting.

The program is available, upon request to the Executive Office of the International Academy of Proctolgy, 43-55 Kissena Boulevard, Flushing, New York.

Dr. Emile Holman Awarded Yandell Medal

On November 11, 1953 the Louisville Surgical Society awarded the first annual David W. Yandell Medal to Dr. Emile Holman, Professor of Surgey at Stanford University, San Francisco.

The annual award and lectureship were instituted to honor the memory of David W. Yandell, founder of the Society, who was Professor of Surgery in the University of Louisville School of Medicine from 1869 to 1898.

Several surgical conferences were conducted at the University of Louisville by Dr. Holman preceding his presentation of the annual Yandell Lecture.

Meeting of the American Psychosomatic Society

The American Psychosomatic Society will hold its Eleventh Annual Meeting at the Jung Hotel in New Orleans on Saturday and Sunday, March 27 and 28, 1954.

Library Contributions for India

The Librarian of the St. George's Hospital Library and Reading Room in South India has requested that members of the National Gastroenterological Association and subscribers to The American Journal of Gastroenterology please forward reprints of published articles for the use of their library.

Medical literature is scarce and anything of this nature sent will be appreciated. Address all material directly to:

Librarian
St. George's Hospital Library and Reading Room
Punalur, P.O.
Travancore, S. India

In Memoriam

MAX EINHORN, M.D.
(1862-1953)

– "When the stream
Which overflowed the Soul was passed away
A consciousness remained that it had left
Deposited upon the silent shore
Of memory images and precious thoughts
That shall not die, and cannot be destroyed".

Doctor Max Einhorn—Honorary Fellow of the National Gastroenterological Association, a founder (1897) and the third president (1899-1900) of the American Gastroenterological Association, and the second recipient (June 1942) of the Julius Friedenwald Award, a pioneer American Gastroenterologist of world-wide fame during a period of more than five decades (about 1890-1940), of active interest in the advancement of gastroenterology as a specialty, died peacefully on September 25, 1953.

"Life's race well run
Life's tasks well done
Rest comes at last".

Doctor Einhorn during his active years believed in work—in addition to a very busy practice and large clientele, he found time for much research, inventions, and the publication of many scientific papers and several books, all of which were widely read, and favorably considered.

"Exegi monumentum aera perennius." The modern majesty consists in work, and what a man can do is his greatest ornament". (Thomas Carlyle—1795-1881).

Doctor Einhorn was well read, a mild mannered simple-life scholar and investigator, and an able clinician and gastroenterologist.

He was –

"Rich in saving common sense,
And, as the greatest only are,
In his simplicity sublime".
(Tennyson in his "Ode on
the Death of the Duke of Wellington").

My friend for more than forty years, whom I admired highly, since my student days at the University of Pennsylvania (1905-1909), and whose writings, and wise words, were always rich and informative mental pabulum for me, as a student and as a clinician and gastroenterologist, over these many years—has gone the way of all flesh, to his everlasting and deserving heavenly reward—with "no distemper, with no blast", – – –

"he fell like autumn fruit
that mellowed long – – –
Till like a clock worn out with eating time,
The wheels of weary life at last stood still".
(Dryden and Lee's "Oedipus").

May I close with Napoleon's famous remark—*"Great men are like meteors, which shine and consume themselves to enlighten the earth".*

May he rest in peace!

HYMAN I. GOLDSTEIN, M.D.

G. RANDOLPH MANNING, M.D.

(1873-1953)

The death of Dr. G. Randolph Manning on December 1st, 1953 was a distinct loss to the National Gastroenterological Association, and to Medicine. He was very active in the early days of the Association, serving as its first president, and since then continuously with distinction in the organization in one capacity or another.

He was a person of vast personal charm, clear vision, and a fine example of dignity at all times. He was respected by his many colleagues to whom he always manifested a friendship and kindliness.

He belonged to a number of organizations, among which were those of organized medicine, and he served with distinction as teacher and professor in the Gastroenterological Department of the New York Polyclinic Medical School and Hospital.

In expressing our sympathy to Mrs. Manning, the National Gastroenterological Association desires to express to her our appreciation of the valuable service her husband gave to our organization, and to acknowledge our loss as deep and continued. May he rest in peace and with the continued regret of those he leaves behind.

ANTHONY BASSLER, M.D.

BOOK REVIEWS FOR GASTROENTEROLOGISTS

DISEASES OF THE LIVER, GALLBLADDER AND BILE DUCTS: S. S. Lichtman, M.D., F.A.C.P., Assistant Professor of Clinical Medicine, Cornell University Medical College; Assistant Attending Physician, New York Hospital; Adjunct Physician, Mt. Sinai Hospital; Assistant in Postgraduate Medical Instruction, Unversity Extension, Columbia University, New York, N. Y. Third Edition in two volumes, thoroughly revised with 220 illustrations and 3 color plates. Volumes 1 and 2. 1315 pages with extensive references after each chapter and an excellent cross-index. Lea and Febiger, Philadelphia, Pa., 1953. Price $22.00 per set.

My compliments to Dr. Lichtman who within several years had the energy and ambition to bring his book on liver diseases up to date and into the third edition. Congratulations are also due to the publishers who have spared no expense in the printing, illustrating and binding of these two volumes.

As to the contents, words are inadequate to describe the valuable information which the reader will find in pursuing these volumes.

The reviewer highly recommends these two books as an essential must to physicians with their already overstacked library.

MODERN CONCEPTS IN MEDICINE: by Julius Jensen, Ph.D. (in medicine) University of Minnesota, M.R.C.S. (England), L.R.C.P. (London), St. Louis. 636 pages. Illustrated, C. V. Mosby Company, St. Louis, 1953. Price $11.50.

This interesting work begins with an "Overture" on A Functional Approach to An Integrated Concept of Medicine. Osler is quoted in the Introduction (Part I, Chapter I): "By the historical method alone can many problems in medicine be approached profitably". ("Books and Men", in Equinimitas).

This "Overture" was originally published in Professor Erik Warburg's Festshrift. *Acta Med. Scandinav. Suppl. 266, Copenhagen, 1952.* Much of historical interest appears in this first chapter. The author discusses the principle of adaptation; early intermediate and final stages of metabolism; regulation of temperature; the kidney; and facility for the excretion of metabolic products; structural responses to the immune reaction. Under "The Transportation System" (Chapters 18 and 19), the blood and the heart and the treatment of heart diseases are particularly well presented in a most unusually fascinatingly informative manner! Enzymes, vitamins, endocrines, and the nervous system and some of the more common nervous disorders are briefly discussed.

The reviewer recommends this well-written work to all physicians. Medical students, internes and residents may profitably study this volume!

DIE BEWEGUNGSBESTRAHLUNG: F. Wachsmann, M.D. und G. Barth, M.D., Universitat Erlangen. Eighth Edition. 192 pages, 124 illustrations. Georg Thieme Verlag, Stuttgart, 1953. Price DM 36.

For radiotherapists, this well written and illustrated monograph will be a welcome addition, provided they are well versed in the German language. A book of this type should be translated into several languages.

On page 178, the reader will find a description and illustration showing the Graaff-Generator and the rotating chair used in the Royal Cancer Hospital, London.

THE BIOCHEMISTRY OF GASTRIC ACID SECRETION: Edward J. Cosway, M.D., D.Sc., F.R.S. 185 pages, illustrated. Charles C. Thomas, Springfield, Ill., 1953. Price $6.50.

Medical students, research workers and many physicians interested in gastric secretion and its chemistry will find useful information in pursuing this concise and comprehensive, though small, treatise on the biochemistry and physiology on gastric acid secretion.

PEPTIC ULCER, PAIN PATTERNS, DIAGNOSIS AND MEDICAL TREATMENT: Lucian A. Smith, M.D. and the late Andrew B. Rivers, M.D., with foreword by George B. Eusterman, M.D. 576 pages, illustrated. Appleton-Century-Crofts, Inc., New York, N. Y., 1953. Price $12.50.

Here is a well written and illustrated volume by men who had the opportunity to see many patients coming to the Mayo Clinic. These patients were of many nationalities and races. They all underwent thorough physical examinations supplemented with laboratory and x-ray studies. Operation, autopsy and study of the removed specimens yielded a mine of information.

Among the recent books written on gastroenterology, liver disease, ulcer, etc., this monograph should receive its merited place in medical literature.

DIE PSYCHIATRIE DES MORBUS ADDISON: W. A. Stoll, M.D., Oberartzt der Psychiatrischen Universitats Klinik, Burgholzl. Eighth Edition. 144 pages, 4 illustrations. Georg Thieme Verlag, Stuttgart, 1953. Price DM 18.

This small monograph deals with the psychiatric aspects of Addison's Disease and is highly scientific. It has extensive references relating to this subject.

Psychiatrists and neurologists who can read German will find this small brochure valuable.

DAS INSELSYSTEM DES PANKREAS: Helmut Ferner, Apl. Professor am Anatomischen Institut der Universitat Hamburg. Twelfth Edition. 186 pages, 54 illustrations. Georg Thieme Verlag, Stuttgart, 1952. Price DM 29.70.

This well written and well printed monograph on the Islands of Langerhans with an extensive reference is recommended to medical students and research workers who read German, rather than to general practitioners. Physicians who specialize in diabetes will also find material relating to their specialty.

DAS ULKUS DES MAGENS UND ZWOLFFINGERDARMS: H. Ramb, M.D., Chefartz der Chirurgische Abteilung Am Laurentius-Hospital, Essen-Steele. Fourth Edition. 68 pages, 28 illustrations. Georg Thieme Verlag, Stuttgart, 1953. Price DM 6.50.

This is one of the many German publications dealing with a particular subject in its entirety. It is a compilation rather than an original essay dealing with ulcer of the stomach and duodenum. Theory, cause and differential diagnosis of the ulcer patient by means of blood serum, etc., complete the essay.

It is interesting reading but nothing new added as compared to recent American texts.

KLINISCHE FEHLDIAGNOSEN: Prof. Dr. M. Burger, Director der Med. Universitats Klinik, Leipzig. Twelfth Edition. 480 pages, 209 illustrations. Georg Thieme Verlag, Stuttgart, 1953. Price DM 58.50.

Errors and/or failures in diagnosis is a well written and superbly illustrated volume dealing with the entire human body. It is divided into 21 chapters, each chapter dealing completely with the organ or system involved. Unfortunately, the average physician is not versed in the German language and is unable to avail himself of this practical and useful volume.

For those physicians who read German, the reviewer recommends this highly practical book as an essential part of their library.

1953-54 YEAR BOOK OF MEDICINE: Edited by Muschenheine, Castle, Harrison, Eusterman and Williams. 736 pages, illustrated. Year Book Publishers, Inc., Chicago, Ill. 1953. Price $6.00.

Quoting from the circular issued by the publishers, "in order to eliminate past confusion these new volumes issued will indicate their publication during the series year beginning September 1953 with issuance of The Year Book of Medicine and ending May 1954 with The Year Book of Pathology and Clinical Pathology".

As in previous editions, articles of importance and interest are abstracted from

medical journals and placed in their respective categories: Infections; Chest; Blood and Blood Forming Organs; Digestive System and Metabloism.

In addition to an extensive cross-index, an index of authors completes the volume.

For the busy physician, The Year Book of Medicine brings to his desk information which he would miss otherwise.

ENCYCLOPEDIA OF ABERRATIONS—A PSYCHIATRIC HANDBOOK: Edited by Edward Podolsky, M.D., with a foreword by Alexandra Adler, M.D. 550 pages. Philosophical Library, New York, N. Y., 1953. Price $10.00.

There are 59 contributors in addition to the editor. Psychiatrists, phychoanalysts and neurologists will be delighted with the wealth of theories and facts found in this well written and enlightening book dealing with aberrations.

The alphabetic arrangement, a to z, definitions and details kept the reviewer's interest at a high pitch.

The editor, Dr. Podolsky and the publishers are to be congratulated on the painstaking preparation of this interesting volume. The reviewer recommends it highly to physicians, even though they may not be psychiatrists.

FIBROCYSTIC DISEASES OF THE PANCREAS: Martin Bodian, A. P. Norman and C. O. Carter. 254 pages, illustrated. Grune and Stratton, New York, N. Y., 1953. Price $6.50.

Fibrocystic Diseases of the Pancreas is a well written and illustrated book. The theory advanced by the authors is, that the respiratory tract, the pancreas and the liver are affected by this congenital disorder.

The use of aureomycin is advocated, although at the present time there is no definite therapy known which would overcome the derangement of the cellular enzyme system.

The pediatrician will find valuable suggestions in this monograph.

SYMPOSIUM ON PRESENT PROBLEMS IN NUTRITION RESEARCH—SYMPOSIUM BASEL 1-4 x 1952: Edited by F. Verzar. 312 pages, illustrated. Verlag Birkhauser, Basel/Stuttgart, 1953. Price S.Fr. 32.

In this volume is found the deliberations of the Fifth International Meeting and Second Scientific Congress on Nutrition.

The list of participants are international and their papers and discussions bring up to date the results of individual and combined research in the chemistry of food, vitamins, hormones, etc.

On page 174, the reader will find a very excellent presentation of the vitamins by Leslie J. Harris, Director of the Dunn Nutritional Laboratories, Cambridge, England. Other interesting and practical discussions deal with free and combined aminoacids in foodstuffs.

MORRIS' HUMAN ANATOMY—A COMPLETE SYSTEMATIC TREATISE: Edited by J. Parson Schaeffer, A.M., M.D., with 15 contributors. Eleventh Edition. 1718 pages with numerous illustrations—black and white and color. The Blakiston Co., New York, N. Y., 1953. Price $16.00.

A half century has passed since the reviewer became acquainted with Morris' anatomy. What a thrill it was then, as it is today, to glance over this splendid volume dealing with the human body. Wonder of wonders how a medical student a half century ago mastered the contents and passed the college and board examination for license to practice medicine.

The new additions in the present text recommend it as far advanced in preparing the medical student for his chosen profession, be it medicine, surgery or one of its special branches.

It is highly recommended.

PROTEINS AND ENZYMES: Kaj Ulrik Linderstrom-Lang. Lane Medical Lectures. Stanford University Series, Medical Sciences, Volume VI. 115 pages, 65 figures. Paper. Stanford, California. Stanford University Press, 1952. Price $3.00.

Beginning with the first Lane lecture in 1896, thirty-one lectures have been delivered at the School of Medicine of Leland Stanford Junior University. This little volume

deals with Micromethods in Biological Research; Distribution of Enzymes in Tissues and Cells; The Initial Stages in the Breakdown of Proteins by Enzymes; The Enzymatic Breakdown of Ovalbumin and Biological Synthesis of Proteins.

For those physicians or research workers who are interested, the reviewer recommends "Proteins and Enzymes" as a most enlightening essay.

THE CONCEPTION OF DISEASE—ITS HISTORY, ITS VERSIONS AND ITS NATURE: Walther Riese, M.D. 120 pages. Philosophical Library, New York, N. Y., 1953. Price $3.75.

This volume is written by a man who has had a great deal, who is steeped in philosophy and who has been associated with many of the great medical faculties of Europe and now is associated with the Medical College of Virginia and other well-known institutions.

It is not for the general run of the mill physicians but rather for those, who like the author, are interested in the higher things in life.

PATHOLOGY: Edited by W. A. D. Anderson, M.A., M.D., F.A.C.P., Professor of Pathology and Chairman of the Department of Pathology, University of Miami School of Medicine; Director of the Pathology Laboratories, Jackson Memorial Hospital, Miami, Florida. With 1241 illustrations and 10 color plates. Second Edition. 1393 pages. The C. V. Mosby Company, St. Louis, Mo., 1953. Price $16.00.

This excellent textbook on Pathology edited by Dr. Anderson is one of the best books available to students, pathologists, surgeons and all physicians interested in pathology, including instructors and investigators in the medical schools and hospitals. The 33 contributors to this fine work are all experts in their fields of interest, and write with authority.

Shields Warren wrote the (18th) chapter on Neoplasms. Ernest M. Hall contributed the chapters on The Heart and The Blood and Lymphatic Vessels. Anderson contributed the sections on The Kidneys, The Pancreas, The Liver, etc. J. R. Shenken and Edward L. Burns wrote the Chapter (26th) on The Gastrointestinal Tract, Maurice N. Richter contributed The Blood and Bone Marrow and The Spleen, Lymph Nodes and Reticulo-Endothelial System (Chapters 31 and 32), and Henry Pinkerson wrote informatively of Vitamins and Deficiency Diseases (Chapter 17). Virgil H. Moon presents an interestingly instructive chapter (Chapter 5) on the Disturbances of Circulation; Professor Enrique Koppisch ably and authoritatively wrote (Chapter 16, pages 358-406) the section on Protozoal and Helminthic Infections.

This textbook on Pathology is enthusiastically recommended by the reviewer for study and daily reference in all medical schools, hospitals, and teaching institutions and to all physicians, surgeons and pathologists.

STRESS INCONTINENCE IN THE FEMALE: by John C. Ullery, M.D., F.A.C.S., F.I.C.S. Obstetrician and Gynecologist, Pennsylvania Hospital; Assistant Professor in Obstetrics and Gynecology, Jefferson Medical College; Associate in Gynecology and Obstetrics, Graduate School, University of Pennsylvania; Chief of Obstetrics and Gynecology, Philadelphia General Hospital; Chief of Obstetrics and Gynecology Delaware County Hospital, Drexel Hill, Pa. 149 pages. Grune & Stratton, New York, 1953. Price $6.75.

The author defines stress incontinence in the female as the loss of urine through the intact urethra, under certain conditions which cause an increase in intraabdominal pressure: as coughing, sneezing, laughing and certain emotions. Sir Eardley Holland first used the term "stress" incontinence.

This small monograph informatively covers the subject satisfactorily and adequately. It will be helpful to the gynecologist and urologist. The author includes interesting historical data on the embryology and anatomy of the urethra, anterior vaginal wall, bladder, and pelvc fascia (Chapter 2, pp. 3-45). There are a number of excellent illustrations (some in black, and some in color).

The publishers issued a handy volume with good paper and clear printing. A bibliography of 137 references concludes the monograph.

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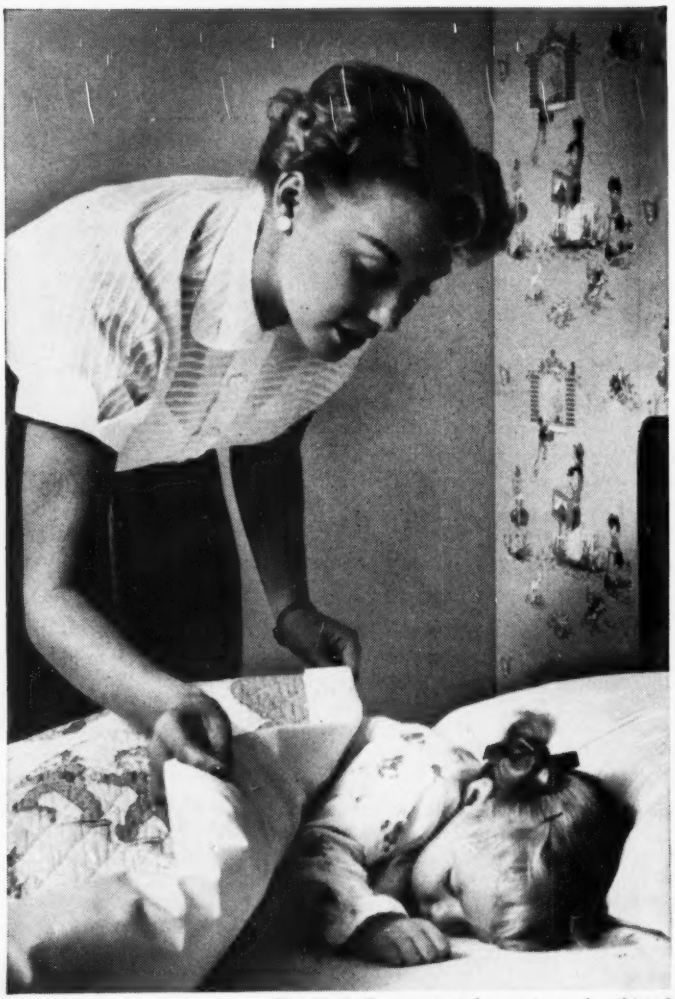

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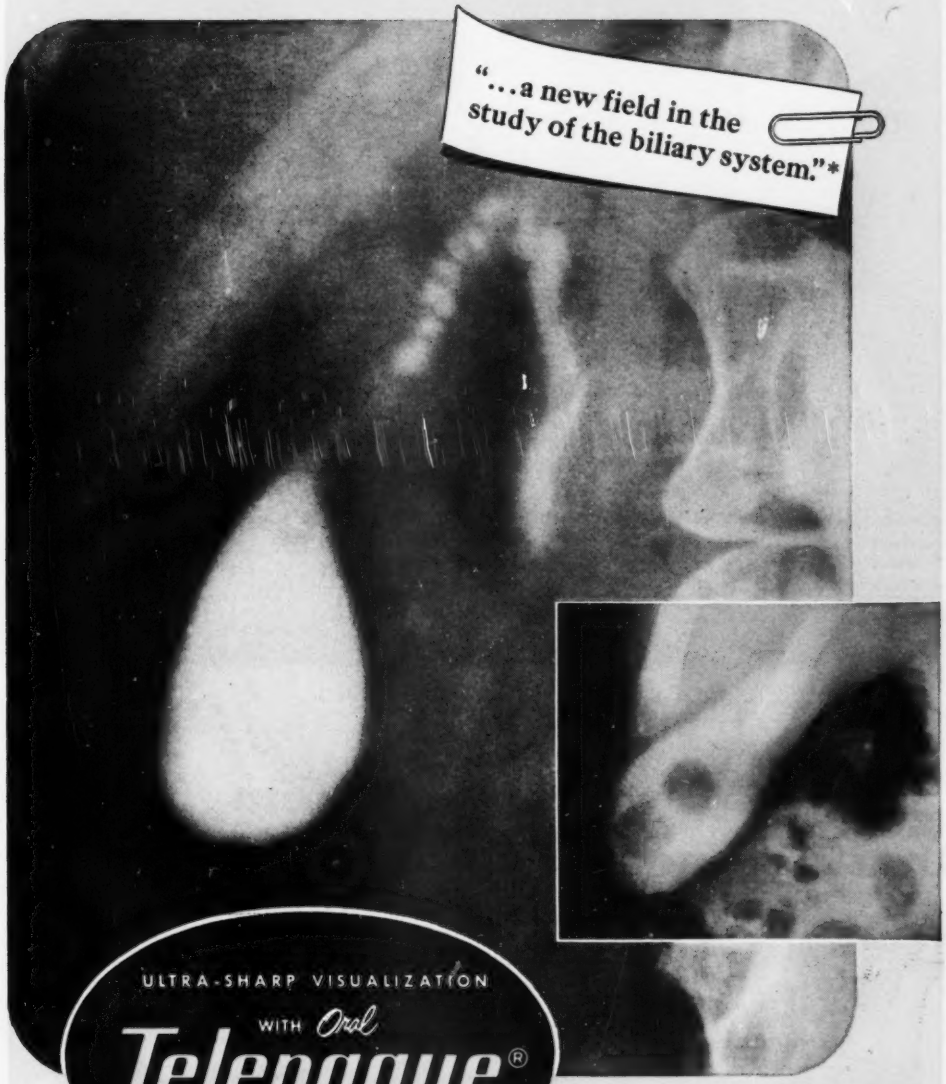

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* Shehadi, W.H.: Am. Jour. Roentgenol., 68:360, Sept., 1952.

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** Steigmann, F., and Goldberg, E., J. Lab. & Clin. Med. 42:955 (1953)

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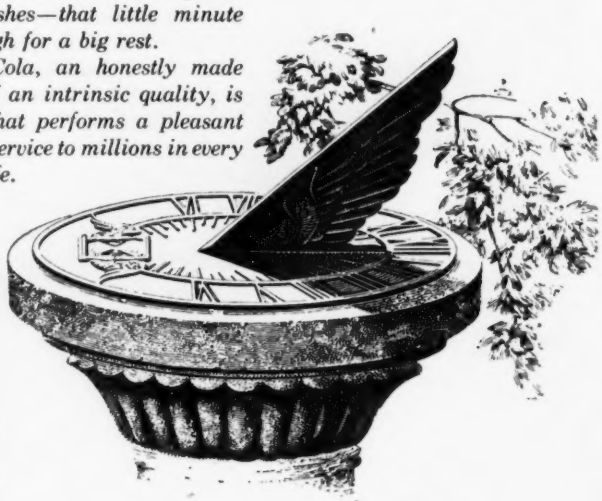

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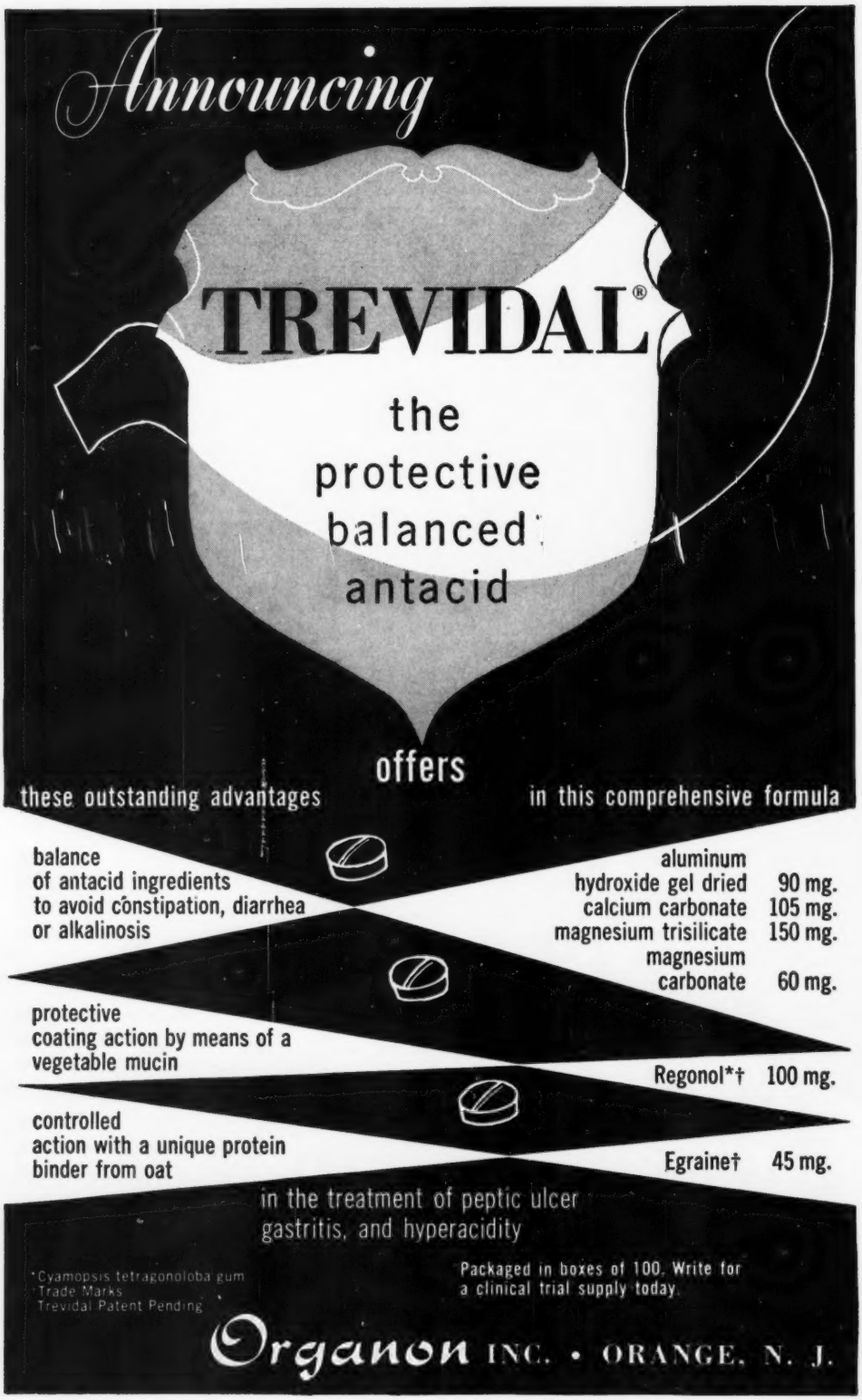
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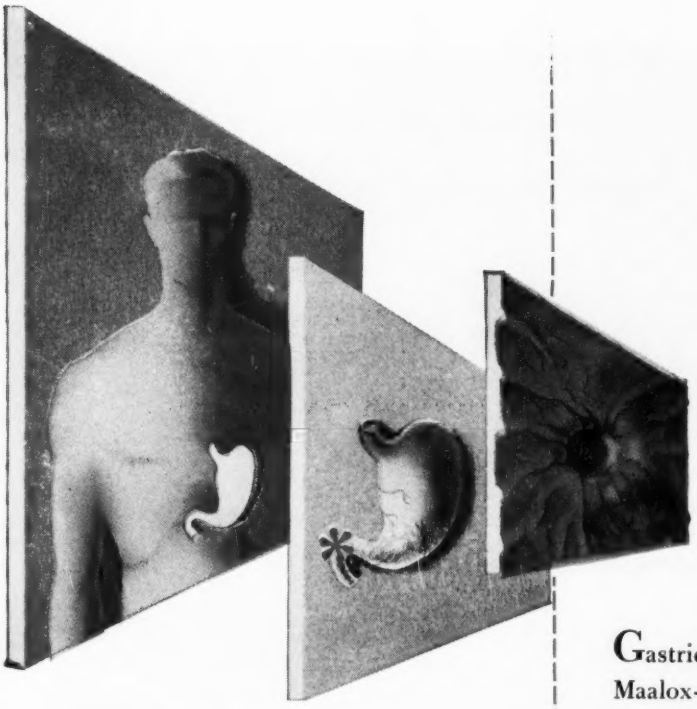

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